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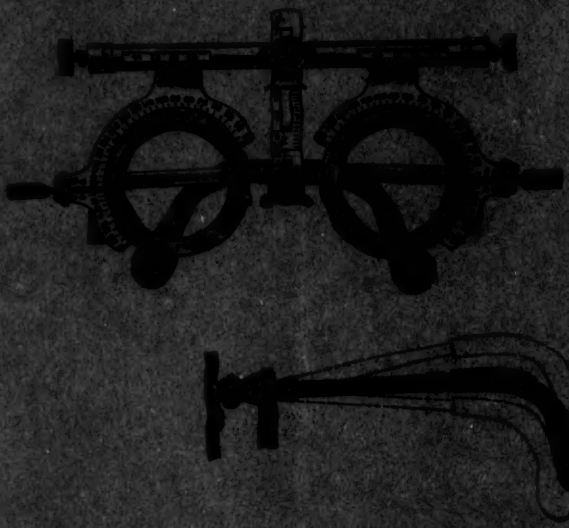

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THE BRITISH JOURNAL
OF
OPHTHALMOLOGY

MARCH, 1947

COMMUNICATIONS

THE COMPARATIVE VISUAL ACUITY AND EASE OF READING IN WHITE AND COLOURED LIGHT*

BY

L. C. MARTIN AND R. W. B. PEARSE

THE subject of visual acuity continues to attract attention. The experimental facts of contour acuity and the certainty of the relatively diffuse character of the light concentration in the retinal image in comparison with the size of the retinal elements, together with the supposed rapid perturbations of the eye direction, have made it reasonable to conclude that visual acuity is dependent on local brightness discrimination, which is known to be a function of the intensity level. We need not here discuss the operation of the retinal mosaic except in so far as it would seem to set a lower limit to resolution under certain special conditions.

The chromatic aberration of the optical system of the eye will render a "white" image somewhat more diffuse than the monochromatic image, and we may reasonably anticipate some improvement of acuity, "other things being equal," in using monochromatic light. Certain measurements of relative visual acuity in monochromatic *v.* white light have, however, yielded contradictory results. The experiments now to be described were not conducted primarily with a view to testing this point, but for a more technical purpose.

* Received for publication, January 10, 1947.

Nevertheless, they may be found of interest in their bearing on the general problem. It was desired to obtain information on the *relative* acuity of an accommodated eye both in red and white light, and also the comparative "ease of reading"; the former presents the more definite problem. The conditions imposed on the work precluded the use of artificial pupils, and binocular vision was used throughout. It was desired, however, to pay careful attention to

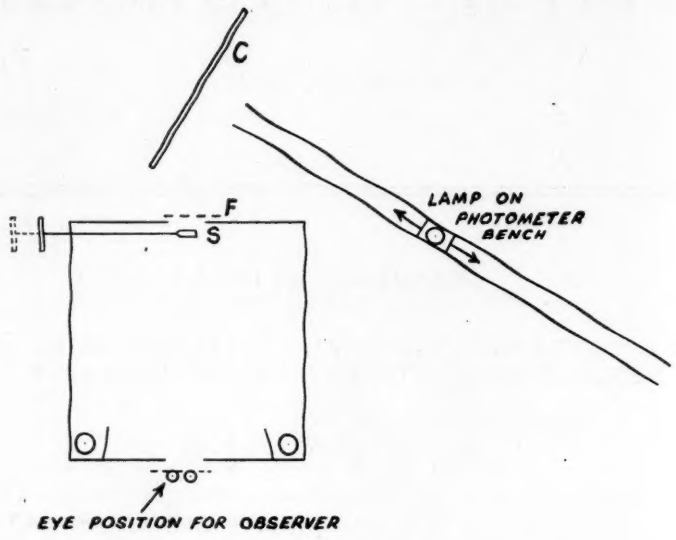

FIG. 1.

the level of brightness of the visual field and the consequent state of adaption of the eye.

The apparatus designed for this purpose, Fig. 1, consisted of a cubical white-lined rectangular box, each edge of which was about 20 in. long. One wall is pierced by the observing aperture (about 3 in. by 1 in.), and the opposite one by a square hole, subtending about 8·5° in the observer's visual field, through which the background C of the acuity object was viewed. The background field was obtained by illuminating a white card by suitable lamps (of colour temperature approximately 2680°K) moving on a long optical bench. The illumination of the white field was measured by a Holophane lumeter. A wide range of illumination levels could be obtained. Red or neutral filters could be placed over the hole at F so as to modify the illumination of the central field. The spectrophotometric transmissions of these filters (Fig. 2) were

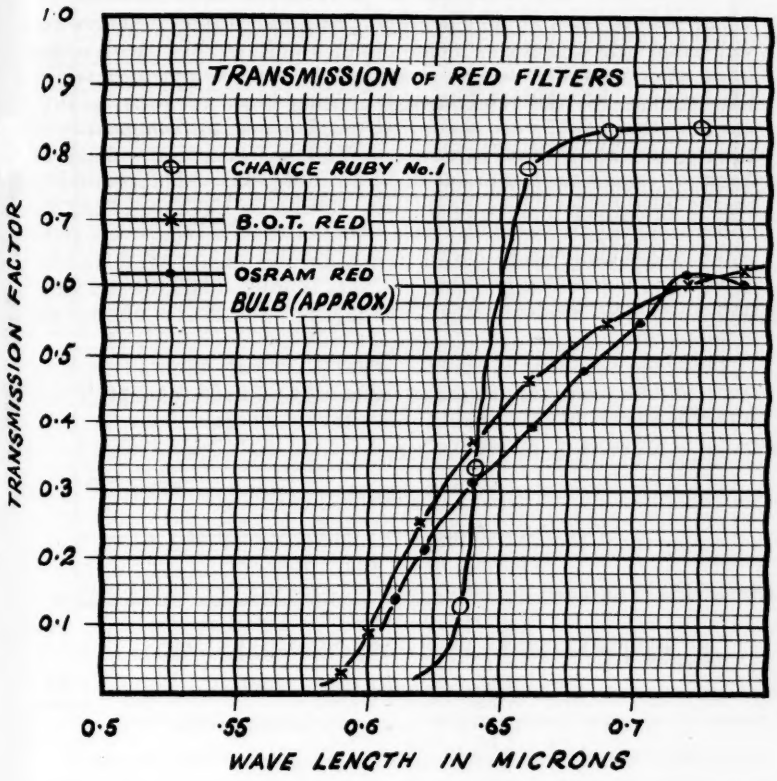

FIG. 2.

measured by the National Physical Laboratory, and their *apparent* light transmission computed with standard photopic visibility data. The white card is assumed to reflect non-selectively.

The specification of the illumination of the field then avoids heterochromatic photometry.

The box contained both red and white lamps screened from direct view, but capable of illuminating the matt-white interior wall of the box (subtending about 30° each way) in which the observing hole is pierced. The illumination level of this wall is thus controlled by screens and rheostats so as to be as nearly equal as possible to and of the same general colour as that of the central field for all observations. The forehead of the observer rested against a velvet-covered stop so that the distance of observation was kept constant.

The acuity object (Fig. 1), was generally a grating; a small transparency about 1 cm. square cut from a lantern slide on which

a half-tone screen (55 lines per inch.) had been printed. There are well-known disadvantages in the use of a grating object with many lines, always parallel to one direction, in any attempt to obtain a fair estimate for the fundamental limiting angle of visual acuity. On the other hand, since the primary object was the *comparison* of the red and white illumination conditions, the great convenience of a grating object seemed to outweigh its limitations. The possibility that a grating may give anomalous results near the threshold by appearing with reversed contrast was not overlooked, and a good many trials were made with a much smaller object of the Cobb type, which seemed, however, to offer undue difficulty to some observers. No evidence that the grating was giving anomalous results came to light.

This object was only adopted after trials with other systems, in some of which reduced images of other acuity objects were projected into the binocular visual field by mirrors or lenses.

TABLE I

Visual Resolving Limit in Minutes of Arc
("B.O.T. Red" and "White")

Observer	Field Brightness Level (Foot-candles)						
	2·64 Red	3·30 White	0·245 Red	0·295 White	Observer*	0 050 Red	0 060 White
2	1·64	1·69	1·94	1·92			
5	1·47	1·57	1·75	1·92			
11	1·48	1·52	1·93	2.14	11	2·32	2·75
13	1·80	1·93	1·89	1·97	15	2·29	2·39
12	1·85	1·96	2·05	2·00	12	2·19	2·15
10	1·65	1·64	1·90	2·00	10	2 27	2·32
3	1·81	1·72	2·10	2·33	3	2·40	2·65
1	2·20	2·20	2·27	2·26	21	2·66	2·73
8	1·90	1·88	2·06	2·08	22	2·77	2·96
9	1·55	1·57	1·71	2·18	20	2·07	2·23
6	2·19	2·22	2·66	2·68	6	2·55	2·60
4	1·75	1·76	1·89	2·21	19	2·46	2·69
Average ...	1·/7	1·81	2·01	2·14		2·4	2·55
Relative Acuity	0·564	0·552	0·498	0·467		0·417	0·392

*The results for the lowest brightness of field with the B.O.T. Red are not strictly comparable with the others, since some of the observers differ. The programme at first included only two brightness levels, and some who took part in the first observations were not available later.

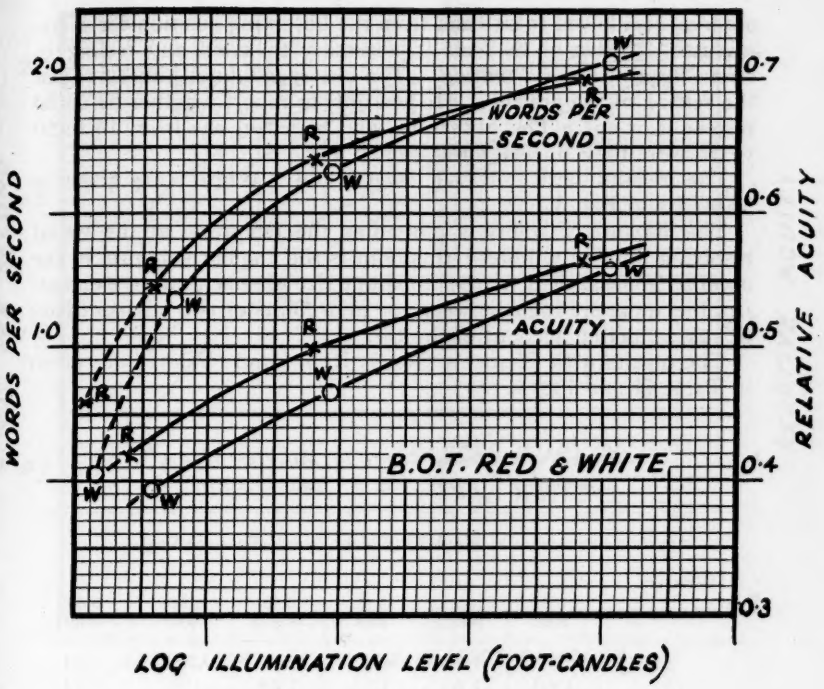

FIG. 3.

Ease of reading and acuity; B.O.T. Red and White.

Comparisons were made between (*a*) white light (*b*) light transmitted by Chance's Ruby No. 1 glass, and (*c*) light transmitted by Board of Trade Red glass. The general levels of illumination used were approximately 0·06, 0·6, 6·0 foot-candles (and for some experiments 3·0 f.c.). Exact values appear in the tables.

The red and white observations were sandwiched, four or five trials being made with white, then with red, then with white again; all for one level of illumination. The illumination was then changed and the procedure repeated.

In the first set of trials the recorder tilted the grating in steps of 10° till the observer reported resolution ceased; he then went back 20° and advanced in steps of 5°; then back 10° and advanced in steps of 2° till the apparent limit was ascertained. However, this system seemed to throw a good deal of strain on the observer, and it was abandoned in favour of finding quickly a first rough setting, and then changing the setting by a degree or two as might seem necessary till the observer feels that the limit is reached. The

observer is allowed to sit back from the observing position for a few minutes as often as he feels it necessary to avoid any feeling of strain in position or attention. The observer did not himself adjust the setting of the grating. He had only to report whether he could resolve it or not. The observers, who varied in age from 14 to 50 years, wore their normal spectacles, if any.

The results with "B.O.T. Red" and "White" are given in Table I and Fig. 3.

The measure of acuity is plotted as the reciprocal of the visual resolving limit in minutes; this limit is the angular subtense in the observer's visual field of the apparent size of one grating element, *i.e.*, the apparent angle between the mid-points of two adjacent bars or spaces, taking account of the tilt.

The results with Chance's 'No. 1. Ruby' and 'White' are given in Table II and Fig. 4.

TABLE II

Visual Resolving Limit in Minutes of Arc
(Chance's "Ruby, No. 1" and "White")

Observer	Field Brightness Level (Foot-candles)					
	6·3 Red	6·3 White	0·66 Red	0·63 White	0·066 Red	0·063 White
8	1·17	1·17	1·35	1·51	2·21	2·31
15	1·60	1·63	1·71	1·98	1·98	2·74
3	1·38	1·46	1·45	1·53	1·98	2·31
10	1·24	1·24	1·36	1·41	1·61	1·82
12	1·07	1·09	1·19	1·16	1·54	1·53
11	1·24	1·20	1·34	1·54	2·03	2·46
24	1·61	1·63	1·68	1·76	2·02	2·32
23	1·98	1·91	1·83	1·77	2·55	2·70
19	1·17	1·24	1·55	1·56	1·79	2·18
26	1·67	1·71	2·30	2·32	2·07	2·41
25	1·52	1·53	1·70	1·74	2·39	2·54
Average ...	1·42	1·43	1·59	1·66	2·01	2·30
Relative Acuity	0·704	0·699	0·629	0·602	0·498	0·435

It was unfortunately not possible to ensure that identically the same group of observers was used for the acuity observations with the two red glasses, moreover the apparent general improvement in the results with the Chance's Ruby glass probably indicates some effects of practice. In spite of the discrepancies between the general averages for the two sets of observations it is probable that the red and white observations have been affected equally.

WORDS PER SECOND

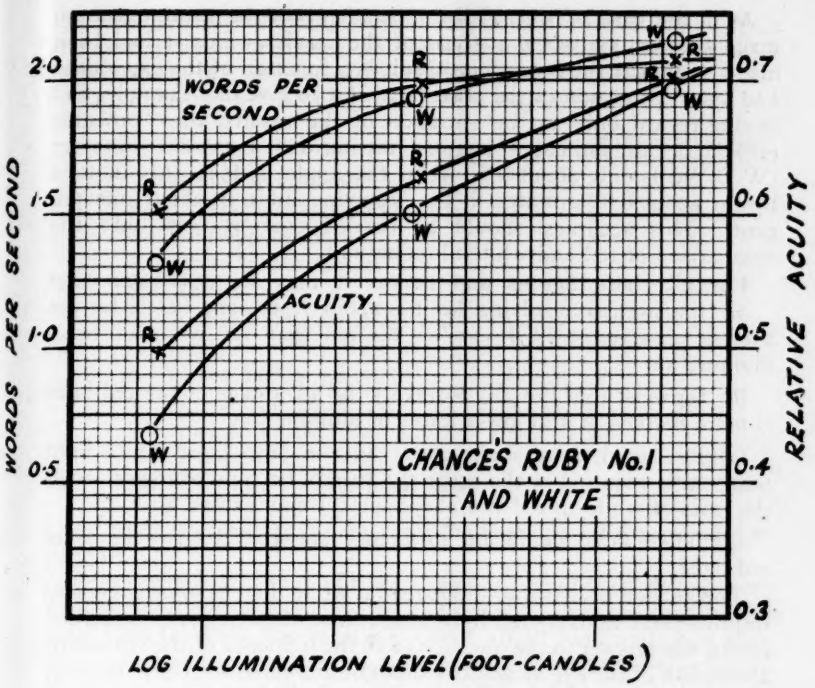

FIG. 4.

Ease of Reading and Acuity; Chance's Ruby No. 1 or White

Some idea of the consistency of the readings (in the second series above) can be obtained from the following table, which shows the spread of the angular settings for three observers picked at random. The columns correspond to the table above.

TABLE III

Difference between Highest and Lowest Angular Settings in Seven Readings together with the Mean Reading

Brightness (approximate foot-candles)	6·0		0·6		0·06	
Observer	Red	White	Red	White	Red	White
25	3/61°	5/61°	5/57°	2/56°	7/40°	8/36°
26	3/58	1/59	7/43	2/60	12/48	4/40
19	3/68	3/67	2/66	2/60	3/46	2/55

As in the case of the reading trials it would be meaningless to make a formal statistical analysis of the results, since it had been made clear that the immediate result is a function of the experience and visual condition of the observer. But to give one example, and having regard only to the variation of the results, the "probable error" of an estimated angular setting for a typical observer (W.D.W.) is only about 0·5° when the angle is 46°; this in turn means about 0·02 minutes in the resolving limit, or about one per cent. This accuracy should be carried over at least into the comparison of red and white illuminations.

For all these figures and curves it may be concluded that

(*a*) the angular resolving limit is about 4 per cent. better for the average observer at 0·6 ft/candles for red than for white of equal illumination;

(*b*) for most (but not all) observers the advantage of the red light is more marked at still lower levels of illumination.

(*c*) For equal visual acuity about 80 per cent. more white light than red is required in the range 0·3 to 0·5 f.c. and at lower levels the ratio of white to red (for equal acuity) may exceed 2 : 1.

(*d*) There is no significant difference between the two kinds of red light.

The general results thus indicate that while there is some suggested improvement in using red light rather than white at low illumination levels, the answer to the question as to the influence of the chromatic aberration of the eye on acuity cannot be answered with any certainty owing to the marked influence of intensity on acuity and the uncertainties of heterochromatic photometry.

The visual acuity of the unaccommodated eye for different colours under conditions of high brightness

The result that intensity rather than colour was the major controlling factor in acuity in the laboratory experiments suggested that acuity of vision when using colour filters in conditions of high illumination might be similarly affected.

Following the experience of the laboratory test, a rotating grating acuity test object was used. It had horizontal lines, and rotated about a horizontal axis. The grating had an element size 16 mm., and was mounted between two opposite apertures in a box through which the grating could be seen against a background of sky. The observer's distance varied from 100 ft. to 140 ft. according to conditions. The front of the box was hidden by a mirror having an aperture 5·8 cm. high and 7·0 cm. wide corresponding to that in the box behind it, and the mirror was adjustable so that it reflected an image of the sky near the horizon behind the observer. In this way

the immediate surrounding field for the acuity object could be given the same general brightness as the sky background. The recorder 'set' the grating, and the observer signalled his observation.

The following filters and goggles were employed:—

Filters	Percentage Photopic transmission (daylight)
1. Kodak hand-shade Yellow	67
2. Kodak hand-shade Orange	30
3. Red eye-shade	16
4. Ilford minus Green	13
5. Neutral goggles	5
6. Kodak hand-shade neutral	3
7. Goggles with plain glass	90
8. Ilford Yellow-green (γ)	45
9. Ilford Blue (804)	40
10. Special double filter (purple) (used as hand-shade	2·2
11. Olive green (946) hand-shade	77

All the filters, except where hand-shade is specified, were used in goggles.

Observations for the high and medium brightness levels were made on the roof of the Imperial College with a general direction of view East to West, and mostly between 10.30 a.m. and 3.30 p.m. (Summer time) so that the sun is to the left. Observers were allowed to shade their eyes from direct sunlight. The 'medium' level observations were made on very dull days.

The brightness of the sky near the acuity object was observed with a Holophane lumeter, but the instrument was working near the top of its range and the readings are approximate only. The readings in apparent foot-candles are given in the following tables. Observations for the lowest brightness were made indoors in a corridor; the grating was seen against a white screen with daylight illumination, and a matt white surround field was employed.

Observations were made for each filter and each brightness level as follows:—

1. Three settings with naked eyes.
2. Three settings with filter.
3. Three settings with naked eyes.
4. Three settings with filter.
5. Three settings with naked eyes.

Thus each figure given in the table for a result "with filter" is the mean of six settings sandwiched between nine settings with naked eyes; the mean of these nine is also entered.

TABLE IV

Angular Resolving Limits (in minutes of arc) with or without Filters

	K.H.S. Yellow 1		K.H.S. Orange 2		Red Eyeshade 3		Ilford "Minus Green" 4		Brightness Levels in foot candles (Sky without filter)			
	with	without	with	without	with	without	with	without	1	2	3	4
1. R.W.B.P.	0·79	0·70	0·79	0·70	1·23	1·04	1·07	1·10	2500	1000	2200	800
2. L.C.M.	0·85	0·89	0·89	0·93	1·22	1·17	1·10	1·20	2500	1000	2200	2000
3. L.B.	0·80*	0·79*	0·70	0·79	0·88	0·57	0·61	0·58	400	400	2500	2500
4. S.	1·45	1·46	1·39	1·44	0·85	0·81	1·10	0·98	2200	2200	700	700
5. A.M.	1·22	0·96	1·27	1·01	1·49†	1·39†	1·37	0·85	800	800	1000	800
6. E.M.M.	2·21	1·92	2·48	1·97	1·46‡	1·39‡	2·33	2·05	1500	1500	1000	1500
7. H.M.	1·44	1·42	1·26	1·31	1·51	1·49	1·22	1·23	2000	2000	1000	2000
8. B.K.J.	1·46	1·48	1·46	1·35	1·27	1·27	1·28	1·22	1900	1900	1900	1900
Mean	1·35	1·26	1·36	1·24	1·24	1·14	1·25	1·15				
1. R.W.B.P.	1·20	1·20	1·25	1·17	1·10	1·02	1·29	1·13	All at 75 f.c.			
2. L.C.M.	1·42	1·45	1·52	1·44	1·71	1·46	1·85	1·50				
Mean	1·31	1·32	1·38	1·30	1·40	1·24	1·57	1·31				
1. R.W.B.P.	1·44	1·53	2·07	1·42	1·96	1·32	2·12	1·32	All at 1·0 f.c.			
2. L.C.M.	2·00	1·84	2·64	1·80	3 24	1·84	3·41	2·03				
3. L.B.	1·17	1·36	1·72	1·24	1·40	1·14	1·96	1·15				
4. S.	1·75	1·60	2·00	1 81	2·85	1·68	3·31	1·63				
5. A.M.	2·32	2·11	2·49	2·32	3·02	2·32	2·80	2·06				
6. E.M.M.	2·40	2·10	2·56	2·18	3·32	2·19	3 06	2·00				
7. H.M.	2·27	2·08	2·88	2·01	2·54	1·59	2·37	1·68				
8. B.K.J.	1·80	1·73	2·55	1·61	2·89	1·44	3·18	1·49				
Mean	1·89	1·79	2·36	1·80	2.65	1·69	2·65	1·67				

*Results below 700 f.c. not included in mean. † Results by L. ‡ Results by E.P

TABLE IV—(*continued*).

	Neutral *Goggles* D=1·3		K.H.S. *Neutral* D=1·5		Plain *Glass* Goggles		Ilford Yellow *Green* (Y)		Ilford *Blue* (804)		Double Filter Purple		Olive Green *Hand-* Shade	
	with	without	with	without	with	without	with	without	with	without	with	without	with	without
1. P.	1·36	1·08	0·97	0·86	1·44	1·43	1·04	1·05	1·02	1·04	1·41	0·85	1·28	1·25
													0·72	0·772
2. M.	1·63	1·24	1·23	0·87	1·18	1·28	1·38	1·38	1·35	1·35	1·99	1·38	1·29	1·24
													1·27	1·32
3. B.	—	—	—	—	0·48	0·58	0·96	1·01	1·14	1·14	—	—	—	—
4. S.	—	—	1·50	1·44	—	—	—	—	1·32	1·31	—	—	—	—
5. M.	1·87	1·27	—	—	—	—	—	—	—	—	—	—	1·20	1·15
6. M	—	—	—	—	—	—	—	—	—	—	3·00	1·98	2·38	2·22
7. M.	—	—	—	—	—	—	—	—	—	—	—	—	1·20	1·24
	1·62	1·20	1·23	1·06	1·03	1·10	1·13	1·13	1·21	1·21	2·13	1·40	1·33	1·31

Brightness levels of Observations above in f. c.

1.	1,000	2,500	1,200	2,000	2,000	1,000	400 1,000
2.	1,000	2,500	2,200	1,000	2,000	1,000	400 1,000
3.	—	—	2,500	2,000	2,000	—	—
4.	—	2,200	—	—	2,000	—	—
5.	800	—	—	—	—	—	800
6.	—	—	—	—	—	1,50	1,500
7.	—	—	—	—	—	—	2,000

The most prominent feature of the observations is the loss of acuity with the majority of the filters; the loss is generally greater, the greater the absorption. Plotting the mean results of R.W.B.P. and L.C.M. for naked eye vision against log. of field brightness a curve was obtained from which the expected increase of angular resolving limit for any filter consequent on it's known diminution of brightness can be roughly found. The data are :—

Illumination in equiv. f. c.	Angular Resolving limit
1,700	0·96
75	1·30
1·0	1·64

Other published data (Lythgoe, Hecht and others) show considerable mutual divergences, and obviously depend greatly on experimental conditions. Our experimental results are therefore retained as likely to apply (better than others) to the conditions special to our work. The following table shows the expected ratio of resolving limits thus anticipated from the loss of light, compared with the observed values; they relate to the highest brightness level only.

Ratio of Resolving Limits

Filter	Transmission factor	Calculated from experimental results	Observed
K.H.S. Orange ...	0·67	1·05	1·07
K.H.S. Yellow ...	0·30	1·14	1·10
Red eye-shade ...	0·16	1·21	1·09
Ilford Minus green ...	0·13	1·23	1·08
K.H.S. Neutral ...	0·03	1·36	1·16
Neutral goggles ...	0·05	1·32	1.36
Ilford Yellow green ...	0·45	1·10	1·00
Ilford Blue (804) ...	0·40	1·12	1·00
Double filter (purple)...	0·025	1·37	1·52
Olive green (AP 946)	0·77	1·04	1·02

The adoption of Lythgoe's results for the variation of acuity with brightness would lead to somewhat smaller 'expected' values; in

fact the 'expected' values for the red eye-shade would fall to 1·13. It may be concluded that as far as the present experimental evidence goes, the whole 'acuity' deterioration caused by a filter may be attributed to the loss of light. This 'photometric' sensitiveness makes outdoor observations very difficult to conduct unless conditions are very steady. Adaptation is very noticeable in the first few moments after putting up goggles or hand-shade, but it cannot be measured with any certainty under the conditions described above.

It may be of interest to note that the observer L.B., who reports extraordinarily small resolving limits as compared with other observers has shown himself to be an exceptionally good rifle shot. In spite of all that has been done on 'acuity', this work suggests that there are still questions regarding effects in daylight (and for particular observers) which are not well understood. The results of L.B. were very consistent, and his estimates were tested over and over again under conditions in which it was impossible for him to know what results his answers would indicate.

Exploratory tests on "Ease of Reading" in Red and White illumination

The general subject of "ease of reading" is one which has received considerable attention from psycho-physical experimenters in connection with investigation of the optimum illumination, size and form of type, and other factors. Apart from the investigation of the possible speed of reading under various circumstances, attempts have been made to register the necessary effort put forward by the reader in terms of "rate of blinking," "muscular tension," "eye movements and the indicated span," "changes in pulse rate" and so on, but it appeared from a first survey of the literature that it would be dangerous to base any experimental conclusion on criteria of the above kind unless as the results of very protracted work. In this case the objective was quickly to obtain a comparison of the ease of reading in equal red and white illumination, and it was decided after consultation with workers who are familiar with such investigations to compare the numbers of simple disconnected words readable in short-period exposures, alternately red and white. Careful consideration was given to the provision of the alternating illumination, and the avoidance of any extraneous factors (such as glare from a page of paper, etc.) which might, if undetected, produce an erroneous result.

The reading material consisted of plainly printed simple words arranged in 15 groups and photographed as lantern-slide transparencies. The slide could be placed in a holder over the viewing hole at S, Fig. 1. The order for exposure of five or seven of the groups was selected arbitrarily before any seven tests; the colour was changed between each group.

The observer, looking through the observing aperture, saw the surround field and fixated a small mark about 10° below the lower edge of the reading field; the latter was quite dark until a switch actuated by an 'Advertisement' motor was mechanically closed for a fixed time of about seven seconds.

The observers were asked to read at such a speed that they felt reasonable accuracy would be possible; occasional casual errors were not heeded in recording the number of words read. The selection and order of the groups, and the order of the relative illumination levels differed from person to person. These precautions, together with the sandwiching of red with white observations, should result in the ultimate elimination of the effects due to 'experience' and the inevitable effects of variations in the reading material.

There is a noticeable lag in the starting of reading after the appearance of the light. Once the reading starts, the observer does not feel much difference of effort between, say six foot-candles and 0·6 foot-candles, but it is considered that the eye movements involved in normal reading, in going from the end of one line to another, are likely to be hindered by loss of illumination; this may be compared with the difficulty in commencement of reading when the light is switched on. The initial lag may therefore fairly be regarded as a part of the test and not merely as an error.

The results for several observers using the B.O.T. Red alternately with white, and Chance's Ruby No. 1. alternately with white are given in the following tables; see also Figs. 3 and 4.

TABLE V

Average Number of Words per Second "Red (B.O.T.)" and "White."

Observer	Level of illumination (Foot-candles)							
	2·64 Red	3·30 White	0·245 Red	0·295 White	0·060 Red	0·072 White	0·034 Red	0·038 White
6	1·85	1·82	1·85	1·88	1·16	1·12	0·78	0·51
4	1·88	1·92	1·92	1·96	1·51	1·51	—	—
2	1·88	2·03	1·72	1·47	1·02	0·86	—	—
5	2·33	2·19	1·65	1·51	—	—	—	—
11	1·96	2·13	2·12	1·78	1·19	1·30	—	—
13	2·23	2·13	1·85	1·92	—	—	—	—
12	2·47	2·47	1·69	1·92	1·48	1·33	—	—
10	2·33	2·19	1·69	1·58	1·37	1·37	—	—
15	1·33	1·72	1·23	1·19	—	—	—	—
8	1·78	1·85	1·36	1·44	0·71	0·59	—	—
9	1·96	2·22	1·58	1·55	1·37	1·37	—	—
Mean for all observations	2·00	2·05	1·70	1·65	1·23	1·18	0·78	0·51

TABLE VI.

Average Number of Words per second "Chance's Ruby, No. 1 and "White"

Observer	Levels of illumination (Foot-candles)					
	6·3 Red	6·3 White	0·66 Red	0·63 White	0·066 Red	0·066 White
8	1·92	1·88	2·20	2·10	1·0	1·09
15	2·22	2·33	2·10	1·85	1·58	1·37
10	2·10	2·13	2·10	2·12	1·19	1·16
12	2·58	3·19	2·30	2·20	1·72	1·47
11	2·24	2·33	2·01	2·22	1·41	1·12
24	1·33	1·34	1·58	1·51	1·40	1·27
23	1·82	1·71	1·74	1·72	1·74	1·64
19	2·22	2·33	1 99	2·01	1·54	1·37
26	2·15	2·19	1·82	1·78	2·03	1·78
25	2·19	2·05	2·01	1·18	1·40	0·82
Mean	2·08	2·15	1·98	1·93	1·50	1·31

In estimating the precision of the results, typical values as obtained by one observer (J.P.) may be quoted. Results are the actual numbers of words 'read' in the trials; all of the same duration.

Approximate illumination level, foot-candles					
0·06		0·6		6·0	
White	Red	White	Red	White	Red
7		17		17	
	12		15		17
11		15		16	
	9		14		16
8		15		18	
	10		15		16
7		18		17	
Mean 8·2	10·3	16·2	14·7	17·0	16·3

The number of results is insufficient for any satisfactory statistical analysis, and indeed the numerical results for speed of reading represent a quantity which depends on very complete psychological factors. However, the quick alternation between white and red was

an effort to secure that whatever the uncertainty in other things, any difference between these illuminations should be brought out. The numerical results suggest that his reading speed is being measured by each observer under any one set of conditions with an error which does not often exceed one word in 7·3 seconds or 0·14 words per second. If there be an average reading speed for human beings it certainly cannot be found from experiments from ten to twelve observers; on the other hand if there be any consistent difference for red and white it should remain (like the effect of varying brightness) after averaging for such a number.

It may be concluded that ease of reading and relative acuity show similar variations under the conditions of these experiments. In particular:—

(*a*) Any difference between red and white illumination in their effect on ease or speed of reading is too small to be certainly established in the present experiments at levels of 0·3 or 6·0 foot candles, though there is some indication that "white" may have some advantage at the higher and "red" at the lower of these two levels.

(*b*) The speed of reading at the lowest intensity (0·06 foot candles) is about 15 per cent. greater for red than for white at equal illumination levels. For equal reading speeds it is necessary to have about 60 per cent. more white than red light.

(*c*) There is no appreciable difference between the two types of red light at any level.

The effects of variation with intensity agree fairly well with "speed of reading" data published by Luckiesh, Taylor and Sinden (*Jl. Franklin Inst.*, Vol. CXCII, p. 757, 1921).

As mentioned above, the purpose of these experiments was of a practical nature, and no attempt was made to use artificial pupils. The eye is under-corrected for both colour and spherical aberration, but the zone of maximum under correction is of radius 1·5 to 2·0 mm. Changing from white to red illumination will remove the chromatic aberration, and call for an increase of about 0·5 D in the effort of accommodation; this is likely to result in a small contraction of the pupil, which would improve the definition but lower the illumination as compared with any possible experiments using artificial pupils.

It is not known whether there was any change in pupil size consequent on changing from red to white, or vice versa, in our experiments.

Only one case of marked colour defectiveness, No. 26, deuteranomalous, was known amongst our observers, though a formal test of colour vision could not be given to all. It is well known, however, that 'normal' individuals differ somewhat among themselves in the apparent luminosity assigned to deep red light ($\lambda > 0{\cdot}65\mu$) as compared with white. If it had been possible to find the relative acuity

etc., with respect to the true apparent luminosity in all cases, the results might have been considerably modified. It is possible that the small relative advantage in acuity and ease of reading associated with red light can be attributed to the improved definition and contrast of the monochromatic image, but there does not appear to be any ready explanation of the tendency of this advantage to disappear, and even reverse, with increasing intensity. The Complex factors are at work which effectively prevent any hasty judgment as to the relative merits of red and white illuminations for acuity and ease of reading. Acuity is, however, not the only desideration for ease of reading, as soon appears from subjective texts.

Subjective tests of reading in red illumination

1. For the first part of these trials a number of red electric lamp (G.E.C. Osram ruby 40 watt) bulbs were procured and loaned to selected individuals with the request that each one should read for half an hour or more in the red light, and give a report of his experience. These bulbs are of ruby glass (not 'sprayed') and the light is largely confined to wave-lengths greater than 0·65μ.

In all cases a reading lamp was employed. An illumination of approximately 0·25 apparent foot-candles can be obtained at about 18 ins. from these lamps with the red bulbs, but they vary among themselves to a considerable extent, and in some cases the illumination did not exceed 0·1 apparent foot-candles.

As a general result of the tests there seems to be no real difficulty in reading at any illumination from 0·1 f.c. (apparent) upwards, except that one or two people find a slight difficulty in ***beginning*** to read. The 'surroundings' seem dark, and there is in some cases a rather vague unfavourable mental reaction— possibly associated with a slight degree of extra effort at the 0·1 f.c. level. Those who tried reading at higher illuminations did not mention any difficulty; it seemed considerably more attractive to read at 1·0 f.c. than at 0·1 f.c.

The para-fovea is well known to be less sensitive to red light as compared with the shorter wave-lengths, and the surroundings appear very feebly illuminated as compared with the book. This again makes conditions seem a little unfamiliar. It may be expected that red light will not be very satisfactory (from a "safety" point of view) in the neighbourhood of machinery, etc.

Some efforts were made in the subjective tests to determine how many words could be read in red light in 15 minutes as against white, but it was found that the uncertainties associated with the variation of the reading material, the changing adaptation of the observer, the effect of practice and so on, were so great as to mask any difference attributable to the change of colour of the light, and the attempt was abandoned in favour of the short-period exposure tests which have been described above.

ALLERGY TO ENDOGENOUS HORMONES AS A CAUSE OF KERATITIS ROSACEA*†

BY

B. ZONDEK, J. LANDAU *and* Y. M. BROMBERG

From the Gynaecologic and the Ophthalmologic Departments of the Rothschild Hadassah University Hospital, and the Hormone Research Laboratory of the Hebrew University, Palestine.

ZONDEK and Bromberg[1] have found that patients suffering from typical allergic symptoms (asthma, rhinitis vasomotoria, urticaria, angioneurotic oedema, etc.) and certain other complaints not usually classified as such (premenstrual tension, pruritus vulvae, migraine, etc.) show in a certain percentage of cases hypersensitivity to their own hormones (" endocrine allergy "). In an earlier paper observations on women with symptoms depending on the genital cycle and related to menstruation or menopause were reported. It was suggested, however, that hypersensitivity to endogenous hormones can also occur in men and women quite independently of genital function.

The condition of endocrine allergy can be detected by an active intracutaneous test. The reaction to a steroid hormone is considered positive when 24-48 hours after intracutaneous injection of 0·1 mg. of steroid hormone dissolved in 0·1 c.c. of specially purified olive oil, a red or pink, slightly elevated and frequently itching papule occurs at the site of the injection. Reactions to insulin (0·1 c.cm.=0·01 units) or gonadotropin (0·1 c.cm.=0·1 units) are read as positive when 1-2 hours after injection of the hormone in physiological saline solution a wide erythema with urticarial swelling occurs at the site of the injection. The characteristic local reaction is accompanied in certain cases by a general reaction (angioneurotic oedema, urticaria, rhinitis vasomotoria, etc.) which affords further confirmation of the diagnosis.

Presence of specific allergy antibodies (reagins) in cases of endocrine allergy has also been demonstrated by the passive transfer test according to Praussnitz and Kuestner, and by spontaneous endogenous passive transfer tests.[1, 2]

The cases selected for the original series of examinations were all of unknown aetiology from a group which had been thoroughly investigated, and in which a condition refractory to treatment had persisted for a considerable period (more than 2 years). In several of the cases desensitisation treatment was applied. Good results were obtained by this means in a large percentage of the group. Details of the treatment and the technique applied have been presented in earlier papers.[1, 2]

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Certain eye diseases of still unknown aetiology (like a case of undetermined keratitis superficialis) were also investigated in the course of this study in endocrine allergy, and good therapeutic results were obtained by desensitisation treatment with allergenic hormones.[1, 2]

The numerous theories of the pathogenesis of keratitis rosacea seem to point to the lack of any definite knowledge as to its true aetiology. It seemed to us that allergy to endogenous hormones might account for a number of these cases.

Keratitis rosacea is characterised by garland-like dilatation of the limbal vessel, vascular invasion of the cornea, and appearance of sub-epithelial opacities in the anterior corneal layers. The opacities gradually increase and finally are apt to cause impairment of vision. The subjective symptoms include photophobia, burning, foreign body sensation, mild pain, and general malaise which disables the patient. Other ocular disturbances, such as blepharitis and conjunctivitis, and rarely keratitis rosacea (and iritis rosacea) are also observed. The syndrome is well-known to occur with or without facial involvement. Rosacea faciei is characterised by appearance on the nose and cheeks of vascular dilatations, initially transient and later permanent, which may lead to a persistent telangiectasia.

The disease is of long duration, progredient in character, and a satisfactory therapy has not yet been devised.

Many theories (contradicting each other), concerning the aetiology of rosacea have been advanced. Bacterial pathogenesis,[3] disturbances in the alimentary tract (hypochlorhydria),[4] and secretory and angiomotor neurosis of a hereditary character[5] have been suggested. A common assumption that the cause of keratitis rosacea is dietary abuse, exhaustion and irregularity in taking meals has been shown to be erroneous.[6]

Recently it has been suggested that riboflavin deficiency is the cause of keratitis rosacea, and may lead at the limbus to vascular dilatation such as is observed in keratitis rosacea. It has been pointed out, however, that the corneal vascularisation due to ariboflavinosis differs from that of keratitis rosacea.[7] The efficacy of riboflavin treatment in keratitis rosacea has been doubted.[8-10]

The obscurity of the aetiology of keratitis rosacea is matched by the uncertainty of its therapy. It is generally recognised that treatment of this condition must be general and constitutional.[11] Local treatment (ichtho-zinc) is only palliative. General treatment has been attempted along different lines, *e.g.*, treatment of possibly present gastric malfunction, protein shock therapy, elimination of septic foci,[11] hormonal treatment with corticosterone,[12] and recently riboflavin.[6, 7, 13]

Tests for presence of hormonal allergy have been performed in

6 cases of keratitis rosacea (3 men and 3 women; duration of disease from 4 to 20 years). All cases were refractory to accepted methods of treatment and showed gradual progress. The six cases of keratitis rosacea were tested with regard to several hormones with the following results: In all of them hypersensitivity to testosterone *only* was found (Fig. 1). Desensitisation treatment with small gradually increasing doses of the hormone produced in every case an improvement of the condition of the patient.

CASE 1.—G.A., female, aged 40 years, housemaid, regular menstrual periods, married for 16 years; three deliveries and one abortion. The father died of diabetes. Two children exhibited

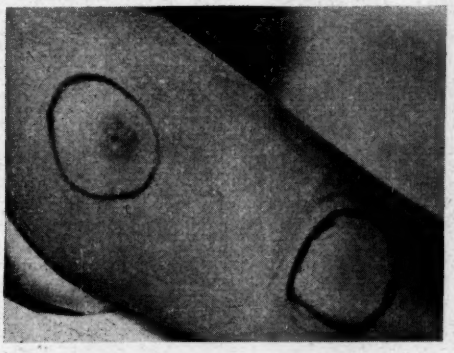

FIG. 1.

Left: Positive intracutaneous test with testosterone in oily solution.
Right: Negative test with oil control.

allergic manifestations. The first child, a 6 year old girl, is suffering from chronic urticaria of unknown aetiology. The second child, a 4 year old girl, suffers from spastic bronchitis. No other peculiarities were found in the patient's history. Rosacea faciei, with symptoms so severe that they were ascribed to lupus miliaris, set in 12 years ago. Concomitantly eye disturbances—blepharoconjunctivitis and keratitis rosacea—developed. The disease gradually became aggravated in the following years, but remissions occurred from time to time. The patient suffered very much from photophobia, burning and lacrimation which disabled her to a great extent. It is noteworthy that all these complaints subsided during pregnancy, but recurred in the period of lactation. There were no other symptoms that could in any way be related to the genital cycle.

Present condition. Extensive rosacea of the cheeks and nose and enlargement of the vessels, were seen giving the face a dark red

aspect; furthermore, bilateral blepharo-conjunctivitis was present, the vessels of the bulbar conjunctiva were markedly enlarged on both sides. The vessels around the limbus presented a garland-like appearance and partly encroached upon the cornea. Sub-epithelial infiltrates, some of them reaching the borders of the pupils, were observed, penetrating partly into the outer layers of the corneal parenchyma (Fig. 2). General examination revealed normal findings: Blood chemistry normal; urine normal; Wassermann reaction in blood negative; blood picture: erythrocytes

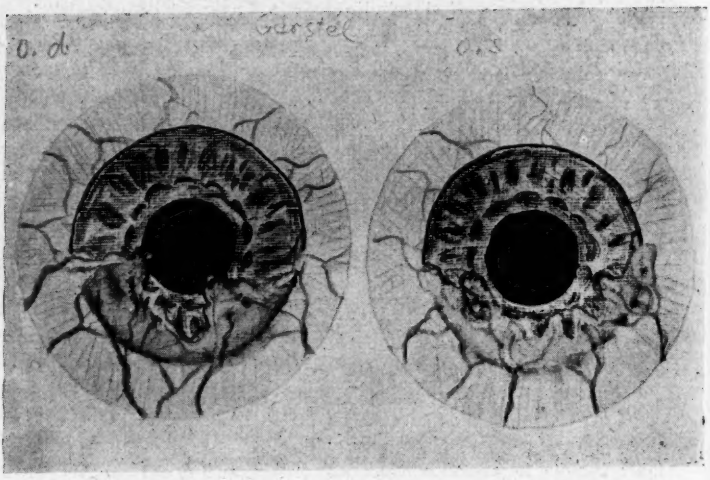

FIG. 2.

Left and right eye: patient (Case No. 1) suffering from keratitis rosacea before treatment. Note garland-like enlargement of the vessels around the limbus corneae.

4,840,000, slight leucocytosis—11,500, eosinophiles 3 per cent., blood sedimentation normal. The following intracutaneous tests for presence of hormonal allergy were carried out:—

(1) ovarian series: oestradiol, oestrone, progesterone, pregnandiol;
(2) adrenal series: corticosterone, testosterone, androsterone;
(3) control series: cholesterol and oil.

The tests showed clearly a strong hypersensitivity to testosterone. Control tests with oil alone and cholesterol were negative. The desensitisation treatment consisted of subcutaneous injections of gradually increased doses of testosterone dissolved in oil (20 successive daily injections of doses ranging from 0·01 to 1 mg.). This therapy produced a definite improvement. The subjective

symptoms of the patient improved, the photophobia disappeared, there was no burning sensation, and the limbal vascular dilatation was considerably diminished. Four weeks after release from hospital, the patient was still free from her former symptoms, and only four weeks later she came to see us with a mild recurrence of the inflammatory symptoms. The corneal infiltrations extended from the nasal limbus to the borders of the pupils and showed characteristic degenerative changes. The patient was again given 10 injections of testosterone (0·1 to 1·0 mg.) and for consolidation of the treatment a tablet of 10 mg. was implanted subcutaneously.

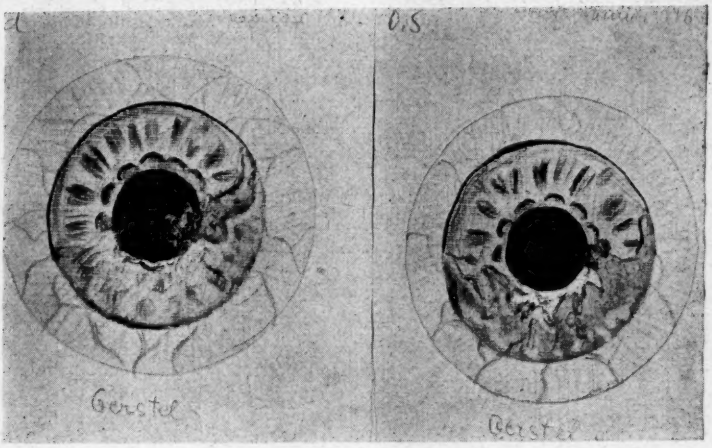

FIG. 3.

Same patient after desensitisation with testosterone. Note recession of the vascular engorgement.

This time the patient remained free from symptoms for a period of 3 months. So long an interval had not previously been experienced by the patient except during pregnancy. Then a mild inflammation set in. 25 mg. of testosterone were again implanted. Ten days after implantation an acute inflammatory reaction was present in both eyes which lasted for two weeks and was ascribed to a possibly excessive dose. Apart from this reaction the patient remained free from complaints. There was considerable improvement of the rosacea faciei. Vascular dilatation in the nose and cheeks regressed markedly, and the face became decidedly less red. Vascular injection of the conjunctiva bulbi and at the limbus diminished. The corneal opacities were unchanged after an observation period of one year (Fig. 3). Local therapy had been avoided as far as possible during this interval.

CASE 2.—K.W., male, aged 45 years, a policeman by occupation. Suffered for many years from chronic dyspepsia possibly as a sequel to chronic amoebiasis. For 6 years rosacea faciei with involvement of the eyes—conjunctivitis and keratitis rosacea. Two years before, the condition of the right eye became so serious that the patient had to be admitted to the hospital. Recurrent ulcers at the temporal border of the cornea were present at that time. Local treatment (cauterisation) and general riboflavin and vitamin A therapy were given. The recurrent inflammation of the eyes greatly hampered the patient at his work.

Present condition. Moderately severe rosacea faciei, bilateral blepharo-conjunctivitis, rosacea, particularly manifest in the left

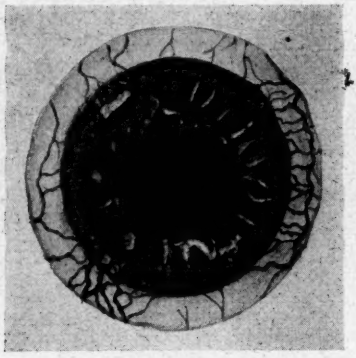

FIG. 4.

Left eye of patient No. 2 with typical keratitis rosacea before treatment. Note strong pericorneal injection of vessels protruding into the cornea.

eye as characteristic vascular dilatations, partly forming a garland over the cornea; the superficial corneal layers were infiltrated (Fig. 4). Wassermann reaction in the blood was negative.

Intracutaneous test with hormonal allergens revealed a positive reaction only to testosterone. The tests were carried out with 0·1 mg. and smaller amounts of testosterone, a positive reaction being obtained even with 0·001 mg. of hormone.

Desensitisation treatment, consisting of a daily subcutaneous injection of a gradually increasing dose of testosterone, ranging from 0·001 mg. to 1·0 mg., was given for one month. The condition of the patient improved and the symptoms disappeared. After two months, mild recurrence of the symptoms was experienced. Ten more injections of testosterone in doses ranging from 0·1 mg. to 1·0 mg. were given, the treatment being consolidated by the

implantation of a pellet of 10 mg. of testosterone. Three months later a second pellet of 10 mg. was implanted. During the period of treatment only transient and mild manifestations lasting 2-3 days were observed. Eventually, a third pellet of 10 mg. was implanted. Local therapy was not employed during the whole time. The condition of the patient improved definitely, as there were no subjective symptoms and the vascular injection receded almost completely (Fig. 5). The rosacea faciei definitely improved as well. The patient, unhampered by any ailment, is again at work. The period of observation was twelve months.

CASE 3.—B.Z., female, aged 62 years, suffered for 20 years from keratitis rosacea accompanied by vascular dilatation on cheeks

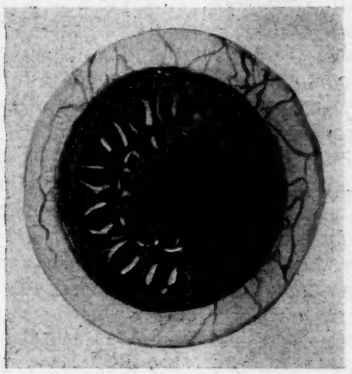

FIG. 5.

Left eye of same patient after desensitization with testosterone. Note disappearance of the vascular injection.

and nose. Recurrences of keratitis rosacea were so frequent that the patient was seriously handicapped in her work. The vessels around the limbus invaded the cornea. Sub-epithelial infiltrates reaching to the pupil area, in both corneae were particularly advanced on the right side. The patient complained of an intolerable almost constant sensation of burning, photophobia and of lacrimation. Intracutaneous tests with several hormonal allergens revealed a strong, positive reaction only in respect to testosterone. Acute inflammatory reaction developed in both eyes during the performance of the tests. Desensitisation treatment with gradually increasing daily doses of testosterone (from 0·01 mg. to 1 mg.) in a series of 20 injections administered subcutaneously was undertaken and finally a 10 mg. pellet of testosterone was implanted. Since this treatment, all the subjective symptoms as well as the

vascular injection receded almost completely. The vascular dilatation on cheeks and nose also greatly improved. During the three months following the conclusion of the treatment, the patient, for the first time in many years, was free from complaints.

The following three cases will be reported briefly as they have been under observation for a short period only; in the first of them desensitisation treament has not yet been instituted.

CASE 4.—R.K., man, aged 42 years, mechanic by occupation, suffered for 5 years from rosacea faciei accompanied by keratitis rosacea. Failed to respond to different treatments, local and general, given during this period. Intracutaneous tests made with different steroid hormones gave a positive response only in respect to testosterone. For personal reasons, it was necessary in this case to postpone the treatment.

CASE 5.—The patient, a woman, suffered from rosacea faciei with keratitis rosacea. The symptoms were of long standing and resisted all earlier attempts at therapy. The intracutaneous tests with steroid hormones revealed hypersensibility to testosterone only. Desensitisation treatment was instituted and produced a marked improvement. (A detailed report on this case will be published by Dr. Lass, Allergist, Hadassah Hospital, Tel-Aviv.)

CASE 6.—A.K., man, aged 65 years, a theological scholar, suffered for the past 17 years from keratitis and conjunctivitis rosacea with a mild facial involvement. Two months previously he suffered from a severe exacerbation of his ocular condition which did not yield to any local treatment. The intracutaneous tests with hormones revealed hypersensitivity to testosterone only. The treatment with gradually increasing doses of testosterone produced a striking improvement at the end of the first week, after which all inflammatory signs receded and the patient was able to resume his work.

Discussion

Allergy is considered to be the cause of a variety of eye diseases. In general the disturbance is ascribed to hypersensitivity of the ocular tissues to exogenous proteins. It has been assumed that human eye tissue can be allergic also to endogenous products of metabolism. In sympathetic ophthalmia, for instance, hypersensitivity to endogenous uveal pigment has been claimed.[14] A positive cutaneous reaction to intradermal injections of uveal pigment extract has been demonstrated in cases of this kind.[15, 16] Histologically cutaneous changes in this allergy resembled the histological changes in the eye.[17] Allergy to endogenous lens protein has also been considered to be a cause of post-operative or post-traumatic endophthalmitis.[18, 19] In our cases it seems necessary to assume the presence in the ocular tissue of a state of allergy

to endogenous hormones. It is of interest that in these cases the endocrine allergic reaction was not directed to protein hormone substances but to steroid hormones of a relatively simple structure. It is remarkable that in the six cases (three men and three women) examined by us the responsible hormonal allergen was always testosterone. This hormone is produced not only by Leydig cells of the testis, but also by adrenal tissue, and this circumstance probably explains the occurrence of an allergy to this substance in mature women. Our findings, pointing in one direction, of course do not exclude the possibility that other aetiological factors may also play a rôle in keratitis rosacea.

Treatment of hypersensitivity to endogenous hormones consists of specific desensitisation by daily subcutaneous injections of the offending specific hormonal allergen, in small and gradually increasing doses and in the present cases with testosterone. All cases showed definite improvement under this therapy. However, mild and transient recurrences were observed after a long interval following the completion of the treatment course. Regular repeated implantations of pellets containing 10 mg. (or may be even less) of the allergen at intervals of 3-6 months are therefore indicated as a means of consolidating the therapy. The initial doses of testosterone employed in desensitisation should be very small, never exceeding 0·1 mg., and the increase should be gradual. These precautions seem to be necessary since focal reactions have been observed after administration of larger doses, as witnessed in our first case. Similar precautions should be observed in pellet implantations.

Therapeutic results in keratitis rosacea must, as a rule, be interpreted with great caution, as spontaneous remissions occur frequently. Nevertheless, the results described above lead us to the conclusion that the treatment was specific. The subjective symptoms improved and the objective signs, the limbal and corneal vascular dilatation, also changed for the better. All patients were relieved, symptom-free periods of equally long duration had not occurred in the absence of treatment or after other treatments. Recurrences were noted in the form of slight vascular injection which, however, receded promptly after a second course of desensitisation with testosterone. An effect on the permanent degenerative corneal changes could of course not be expected.

Endocrine allergy affords a possible explanation for the unknown aetiology of certain diseases. While in some of them the offending hormonal allergen may vary (*e.g.*, in urticaria positive reactions were found with regard to oestrone, testosterone and corticosterone) it is noteworthy that in our small group of cases of keratitis rosacea all showed allergy to one and the same hormone,

Proceeding from the assumption that the ocular tissues are

capable of allergic reaction to endogenous hormones, other eye diseases of obscure aetiology and long duration, and in which an allergic basis could be suspected, have been studied from this point of view (chronic, periodically recurrent conjunctivitis and undetermined cases of keratitis superficialis as well as other diseases[2]). The results obtained in these cases owing to desensitisation treatment with the respective hormonal allergens have been encouraging.

Summary

1. Six patients with keratitis rosacea associated with rosacea faciei (3 men and 3 women) of long duration which had proved refractory to the usual methods of treatment, were examined for hypersensitivity reactions to endogenous hormones.

2. In all cases allergy to testosterone was demonstrated by positive skin reactions to intracutaneously injected testosterone. Other hormones (oestrone, oestradiol, progesterone, pragnandiol, corticosterone, insulin, gonadotropin) gave negative reactions.

3. Desensitisation treatment by a course of subcutaneous injections of testosterone in gradually increased doses and implantation of pellets containing 10 mg. of testosterone propionate produced satisfying results.

4. Testosterone gave relief only when given in low, gradually increased doses; administration of large doses may cause a severe exacerbation.

5. The finding of allergy to endogenous testosterone in a small number of cases of keratitis rosacea does not exclude the possibility :—

(*a*) that other endogenous hormones may act as allergens in some cases;

(*b*) that other causative factors are involved in the aetiology of keratitis rosacea.

The results achieved were as follows :—

(*a*) Complete and prompt cessation of the subjective symptoms, photophobia, lacrimation and sensation of burning in the eyes.

(*b*) Considerable improvement or disappearance of the limbal and corneal vascular dilatation, as well as a marked improvement of the facial rosacea.

(*c*) Mild recurrences in some instances which promptly improved after administration of a second course with testosterone treatment.

We are indebted to Prof. A. Feigenbaum, Head of the Ophthalmological Department, Rothschild Hadassah University Hospital,

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SOME OBSERVATIONS ON THE SYMPTOMATOLOGY AND DIAGNOSIS OF CASES OF PROPTOSIS*

BY

PROFESSOR HANDOUSA BEY

CAIRO

I HAVE had to examine and treat a large number of cases of proptosis, most of them referred to me by the various ophthalmic centres in Egypt. Study of the records of these cases reveals some valuable points worthy of publication.

The types of cases that I have come across, fall into the following categories:—

1.—Cases of Extra-Orbital Causation.
2.—Cases of Intra-Orbital Causation.
3.—Cases due to disease of the bony wall of the orbital cavity.

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1.—Extra-orbital cases

These were mainly of nasal origin and inflammatory in nature. The frontal and ethmoid para-nasal sinuses were the main primary sites and usually the spread took place in an acute case or during an acute exacerbation on top of a chronic one.

Nasal trauma, mucoceles, pyoceles and neoplasms, were not uncommon causes.

Maxillary sinus infection in my cases has never been seen to give rise to proptosis unless the related anterior ethmoid is infected too, a point indicative that the infection has spread from the latter.

Nasal neoplasms causing proptosis were mainly malignant, affecting the ethmoid and maxillary regions. They were either carcinomata, sarcomata, or endotheliomata, with 4 cases of osteoclastomata and 3 cases of adamantinomata.

Nasal neoplasms of simple nature causing proptosis were mainly osteomata. I had only four cases of ethmoid fibromata and two ethmoid haemangiomata.

Nasopharyngeal tumours, whether simple or malignant have been commoner causes of proptosis than usually supposed, a point that stresses the importance of examining the nasopharynx in cases of proptosis of vague causation.

2.—The Intra-orbital category

I included under this heading all the cases in which the causative lesion has started inside the orbital cavity.

These were 31 in number, grouped as follows:—

1. *Inflammatory*—(*a*) One case of amyloid change in the orbital tissues round the globe, most probably secondary to chronic suppuration around the teeth and in the maxillary antra.

(*b*) One case of syphilitic change in the orbital contents on both sides, associated with enlargement of the parotid and submaxillary salivary glands simulating Mikulicz's disease.

2. *Cysts*—(*a*) Intra-orbital dermoids related to the upper eye-lid region.

(*b*) Retention cysts of the lacrimal gland.

(*c*) Haemorrhagic cyst of the lacrimal gland.

(*d*) Parasitic cysts—2 cases of hydatids. One lying inside the muscle cone and one lying outside it related to the orbital floor.

3. *New-growths*—These were the commonest in this category, (23 cases out of 31), 6 were simple, in the nature of fibromata, fibro-lipomata, rhabdo-myoma and lymph-angiomata: The malignant types were sarcomata, carcinomata, endotheliomata and one case of xanthoma. The carcinomata and endotheliomata were all arising from the lacrimal gland, the xanthoma was most probably arising from the tendon of the superior oblique muscle.

3.—Cases due to a disease of the bony wall of the orbital cavity

These were the least common among my group of cases and may be grouped as follows:—

1. *Traumatic*—One case of old fracture of the left maxilla that resulted in a large gap in the floor of the left orbit with the formation of an extensive arterio-venous varix, which pressed on the left globe and induced proptosis on stooping down.

2. *Inflammatory*—(*a*) Pyogenic, of the nature of osteomyelitis (acute and chronic) of the orbital wall.

(*b*) Tuberculous abscesses, and gummatous formations of the orbital wall.

3. *New Growths*—I have one case of capillary angioma of the frontal bone causing right proptosis, a very rare condition.

Study of the symptomatology of these cases shows that in spite of varying degrees of proptosis and eyeball deviations, diplopia is exceptionally complained of. I thought at first that this may be because the patients were more concerned with the bulge of the eye but I directed their attention while being under investigation in hospital to the possibility of seeing double; still this was not complained of except very rarely. Twenty successive patients were carefully tested, only in two diplopia was reported.

As regards diagnosis of the underlying cause of proptosis, I should like to stress that pitfalls with serious consequences are very likely unless careful history taking, systematic local and general examination is carried out in a routine manner, assisted by the various radiological and laboratory investigations. Many demonstrative examples can be given; I have among my cases, patients that were referred to me as having sarcomata of the orbit, with local clinical signs, suggestive of malignant disease, but simple careful history taking made me doubtful and with systematic investigation, these cases proved to be inflammatory. Inflammatory masses in the orbit may closely simulate malignant disease in many clinical aspects.

I have met with few but very valuable points in radiological study of my cases which are worth special consideration. These are:—

1. The pathological lesion in middle and posterior ethmoiditis may spread towards and into the orbital cavity giving rise to proptosis at the same time not presenting any clinical evidence intra-nasally. Even in some of these cases X-ray examination in the classical positions may prove to be negative. However, if this is repeated in various other positions, definite radiological signs may be found to indicate the site of the disease in the ethmoid. I have had two such cases which were considered clinically and radiologically negative for sinus disease and the cause of the proptosis was not then determined. Interest and patience in repeating the X-ray examination cleared up the diagnosis of ethmoiditis.

Fig. 1. is an X-ray which is very definite of left ethmoiditis with thickened bone was only arrived at after repeated negative trials in a case of proptosis.

2. Comparative X-ray study of both orbits has indicated or defined the site of the underlying cause of proptosis in many a case of obscure origin.

I shall stress here only two points—

(*a*) The presence of an X-ray shadow of the tumour mass.

(*b*) The presence of an X-ray shadow of the primary orbital dilation.

(*a*) With appropriate technique not only bony but also soft tissue masses can be demonstrated deep in the orbital cavity. I have cases in which the radiologist has succeeded even in demonstrating the shadows of both eye-balls in normal cases.

This fact was made use of in demonstrating tumours lying far back in the orbital cavity, not palpable or demonstrable otherwise, and is always worth a trial.

X-ray shadows of bony masses are well known; shadows given by soft tissue masses have been of two types: dense and light.

Dense shadows when present were always diagnostic of the underlying cause of proptosis. Fig. 2 is a demonstrative example of such a dense shadow. This patient is an old exophthalmic goitre case in which appropriate treatment resulted in great diminution of his exophthalmos with fall of his B.M.R. from (+45 to −7). It was noticed about one year later that his right eye-ball was again proptosing gradually. Investigations were negative as to the cause, but with careful radiological investigation and comparing both orbits a shadow could be seen in the right orbit (Fig. 2). This on exploration proved to be a rhabdomyoma, removal of which resulted in cure.

Light shadows show as veiling particularly over the orbital periphery. They were always found to correspond with the congested and oedematous orbital tissues and so they demonstrate secondary manifestations and not the primary cause of the proptosis. Fig. 3 is an example of such a shadow.

(*b*) Orbital dilatation has been seen to be produced by many extra- and intra-orbital lesions. For descriptive purpose may I term the former secondary and the latter primary dilatation. In my experience there has been no difficulty in differentiating one from the other.

As an example of secondary dilatation I refer to the X-ray (Fig. 4), in which the dilatation has been demonstrable in the film to be due to a communication between the orbital cavity and the dilated ethmoid. On the other hand X-ray (Fig. 3) shows simple orbital dilatation which is not due to any communication with neighbouring cavities, hence the term "primary dilatation."

Primary dilatation has been found consistent with the presence of an intra-orbital lesion and fully justifies exploration.

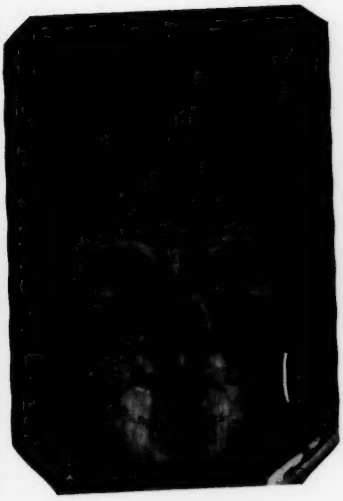

FIG. 1.

FIG. 2.

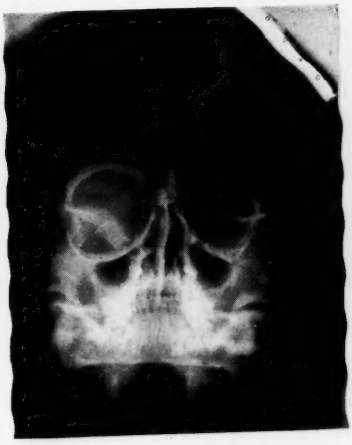

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

This sign was positive in 16 cases out of 21, and was the only evidence of intra-orbital tumour, a case in which a deep fibroma was found and removed on exploration.

It was negative in the following cases, all of which had other diagnostic signs:—

1. One case of osteoma of the ethmoid bone which was lying superficially and was palpable.

One case of myoma.

Both these gave definite X-ray shadows that were diagnostic.

2. One case of fibro-lipoma.

One case of ? Mikulicz's disease.

One case of endothelioma of the lacrimal gland.

In these three a mass could be palpated.

So these radiological findings may be of immense diagnostic value in obscure cases and justify exploration if need be.

Therapeutic tests: have been to me of great value in certain cases and so I feel they deserve trial if need be.

I had a case of a palpable mass in the left orbit firmly adherent to the bone and completely fixing the globe. The clinical signs were very suggestive of a new growth. This patient had an empyema of the left maxillary antrum with left ethmoiditis. On repeated punctures the eye condition improved considerably in 3 weeks. (Compare Fig. 5 and Fig. 6). With sinus treatment the patient was cured. This case demonstrates clearly the value of the therapeutic test (antral puncture).

There are other cases who had a positive Wassermann reaction—anti-syphilitic treatment resulted in resolution of the eye condition and saved major surgical intervention.

Exploration and biopsy has to be finally resorted to in obscure cases.

It has been my routine in any case where the lesion looked malignant on exploration to have a biopsy done before attempting to do radical operations. My case of amyloid disease demonstrates the wisdom of this conservatism. In this case all the appearances during exploration were suggestive of malignancy. If radical treatment was attempted straight out he would have lost the remaining bit of vision in that eye, a vision that is very much needed to him as he has a nebula on the opposite cornea.

Even if, on exploration, malignancy is certain, biopsy alone should be done as it determines the type of malignant disease present; a point which is of the utmost help in planning the line of treatment.

Cyst puncture: As a diagnostic aid has been advised and carried out by many. I am of opinion that it should not be freely done, as aspiration of the cyst contents not only makes the operation of complete cyst removal difficult, but also the procedure of puncture in itself may spread the disease in cases of hydatid cysts and breaking down malignant tumours.

I thank Prof. Sorour Bey and Dr. Hashem for their work on the pathology of my cases. I feel greatly indebted, too, to our expert radiologists, particularly Dr. Nissim Abou Saif and Dr. A. Marey for their valuable radiological study of these cases. I would like to express my deep gratitude to Dr. A. Barbary and Dr. Louis Labib who have assisted me in the operative work and have carried out a large part of the investigations, also to Dr. Ibrahim Mossalem, who has done the drawings, and to Sayed Ibrahim Eff, who has typed this paper.

THE INFLUENCE OF INTRA-OCULAR PRESSURE ON THE RATE OF DRAINAGE OF AQUEOUS HUMOUR. STABILIZATION OF INTRA-OCULAR PRESSURE OR OF AQUEOUS FLOW?*†

BY

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I.—Introduction

THE problem of the stabilization of intra-ocular pressure has aroused much interest. There are theories postulating reflex regulation of some kind or other. These have been critically examined elsewhere (Bárány, 1946 *a*). On the other hand, there are two theories, namely those of Duke-Elder and of Friedenwald and Pierce, which put the burden of stabilization on the mechanism of aqueous outflow.

Based on his elegant determinations of intra-scleral venous pressure in the dog, Duke-Elder (1926) has proposed a "safety-valve action" theory of the aqueous drainage mechanism. According to this theory, the pressure relations between the anterior chamber and the drainage channels are such as to prevent any flow of aqueous at normal intra-ocular pressure. When the intra-ocular pressure is raised, however, the pressure relations are reversed and become favourable for drainage of the aqueous. It is obvious, that any drainage mechanism which permits an increase of aqueous outflow with increasing intra-ocular pressure will, in a certain sense, tend to stabilize the intra-ocular pressure. The efficiency of a mechanism in stabilizing intra-ocular pressure depends on the slope of the curve relating aqueous flow to pressure. If the mechanism is efficient, even a small change in pressure will cause a large change

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†The radio-active sodium used in the experiments was kindly furnished by Prof. Manne Siegbahn, Research Institute for Physics, Stockholm.

in aqueous outflow. The "safety-valve" mechanism of Duke-Elder is one way in which this could be realised without necessitating a large flow of aqueous under basal conditions.

The application of Duke-Elder's theory to other species has been criticised, however, from an anatomical point of view by Troncoso (1942) after a thorough study of the vascular apparatus of the drainage angle. In view of the conclusive demonstration by Ascher (1942) and independently by Goldman (1946) of a continuous aqueous outflow in man and the proof of a considerable outflow under completely physiological conditions in the rabbit's eye by Kinsey and Grant (1942) the theory must probably be modified at least for these species.

It might conceivably be possible to retain the gist of the "safety-valve" theory by restating it as saying that the intra-ocular pressure is stabilized by means of an overflow mechanism.

If the drainage mechanism is to function as an overflow arrangement, which seems to agree with the ideas of Friedenwald and Pierce (1932), two conditions have to be fulfilled. First, the pressure in the drainage channels, as determined by the intra-scleral circulation, must be—if not actually higher than the intra-ocular pressure—at least only a little lower. Second, the resistance to aqueous flow from the anterior chamber to the drainage channels must be very low. If the drainage mechanism acts as an overflow arrangement, then the normal, not inconsiderable flow of aqueous is the result of a small driving force and a small resistance and even a small change in intra-ocular pressure will cause a large relative change in driving force and a large relative change in aqueous flow.

Since at present no means are known for measuring the pressure in the actual drainage channels nor for determining the resistance to flow from the anterior chamber under physiological conditions, the efficacy of the drainage mechanism as a pressure stabilizer can only be tested by direct measurement of the influence of intra-ocular pressure on the rate of aqueous flow.

This has been tried before by Niesnamoff (1896) and by Friedenwald and Pierce (1932). These authors introduced cannulas into living eyes and measured the rate at which normal saline entered the eye at different pressures. For a rabbit's eye Niesnamoff found an inflow of 1 mm.^{3} per minute at 25 mm. Hg and of 5 mm.^{3} per minute at 33 mm. Hg. For dogs, Friedenwald and Pierce found an inflow of 5-10 mm.^{3} per minute at a pressure not more than 5 mm. Hg over the normal level of the anaesthetised dog. In Niesnamoff's rabbit, the intra-ocular pressure was obviously a little lower than 25 mm. Hg, probably about 23 mm. Hg. Thus, a pressure increase of about 10 mm. Hg above normal brought an increase of aqueous flow by about 5 mm.^{3} per minute. Under completely physiological conditions, the rate of flow in rabbits is

about 4 mm.^{3} per minute (Kinsey and Grant, 1942). On a relative scale, therefore, Niesnamoff found an increase of 125 per cent. in aqueous flow caused by an increase of 43 per cent. in intra-ocular pressure. A similar calculation cannot be made for the data of Friedenwald and Pierce because we have no corresponding information about the rate of flow of aqueous in the dog under completely physiological conditions.

However, the results quoted above are open to criticism because they were obtained with a cannula in the anterior chamber of anaesthetized animals, that is on eyes under definitely unphysiological conditions. Moreover, the rabbit data derive from one experiment on one eye only and there might be species and individual differences. It therefore seems justified to take up the question anew. I have therefore used a new method to obtain an idea of how rapidly the aqueous outflow changes with a change in pressure in eyes which have not been subjected to any trauma whatever. Unfortunately, the method does not permit a study of the functional relation over a large range of pressure but only gives the slope of the curve in the vicinity of the normal equilibrium. However, this is the most interesting region from the point of view of physiological regulation.

II.—Experimental part

The principle of the method used is the following:

Under equilibrium conditions the composition of the aqueous is constant. This means that per unit of time, the same net amount of any substance as enters the anterior chamber will have to leave it by means of aqueous outflow or by diffusion. If diffusion plays no part the equilibrium condition is

Net rate of entrance $\underline{E}_o$ of substance=

(concentration $\underline{C}_o$ of substance) × (rate of flow of aqueous $\underline{F}_o$)

If we now change the equilibrium level of the intra-ocular pressure of an eye by some non-traumatic intervention, the corresponding rate of aqueous drainage F_1 can be obtained from the relative change in rate of entrance of a substance and the relative change in its equilibrium concentration.

$$\frac{F_1}{F_o} = \frac{E_1/E_o}{C_1/C_o} \qquad (1)$$

Thus, the experimental problem consists in finding a suitable non-traumatic way of changing the intra-ocular pressure and a suitable substance. Then the related changes in intra-ocular pressure, equilibrium concentration and net rate of entrance of the substance are determined.

In the experiments to be described, the change in equilibrium levels was brought about without touching the eye proper by unilateral closing of the common carotid artery in rabbits. A very large

number of experiments on unanaesthetized animals have shown that, on an average, this reduces the mean blood pressure in the ophthalmic arteries by about 30-40 mm Hg from the normal level of about 100 and the intra-ocular pressure by about 4 mm Hg from the normal level of about 30. The pressures assume new levels which do not change appreciably from 10-20 minutes after closing of the vessel to 24 hours after the operation (Bárány 1946*a*, *d*, 1947*b*).

Carotid closure may appear to be a rather indirect way of changing the intra-ocular pressure. It has the quite invaluable advantage, however, of leaving the other eye unchanged and usable as a control.

The test substance used for the studies was the radio-active sodium isotope Na (24). As Kinsey and Grant (1942) have shown, there is no significant diffusion exchange of sodium between aqueous and blood, sodium enters by secretion and leaves by a process of flow. Consequently, this substance is especially suited for our purposes.[1]

Aqueous samples can be obtained under topical anaesthesia but it is much easier and safer to use general anaesthesia. The question then arises, whether the drug used, allyl-isopropyl barbituric acid, Numal Roche, might influence the relevant relations between levels of concentrations and pressures. In order to avoid possible pitfalls here, some of the experiments to be described were made with intra-peritoneal administration of Numal. In these cases the animals had been under the influence of the drug for up to two hours when the aqueous was withdrawn. In other experiments, the drug was given intravenously only 5 minutes before the corneal puncture. There was no noticeable difference between the results. The pressure effect

[1] The fact that radio-active test substances in the body fluids can be detected by means of counter arrangements outside the body suggests the following possibility for studying the rate of aqueous exchange in the intact eye: By means of a suitable time schedule of injection (if necessary controlled by continuous observation of the plasma concentration with a counting rate meter) a practically constant plasma level of a test substance could be maintained from the very start. The test substance preferably should be a radiator of not too penetrating corpuscles. A counter arrangement subtaining a small "visual angle" and equipped with suitable filters could then be arranged to measure radiation practically exclusively from the cornea and the superficial layers of the aqueous. The accumulation of the test substance in these two compartments could thus be followed. The fluid exchange of the cornea is slow and the total electrolyte content relatively low. Therefore, the initial slope e of the accumulation curve would certainly depend almost exclusively on the rate of accumulation of radio-active substance in the aqueous and thus be a measure of the rate of entrance of the test substance in arbitrary units. After a certain interval, the aqueous concentration would have reached an equilibrium level. If the corneal concentration were still sufficiently low, the radiation from the eye at this juncture would express the equilibrium concentration c of the substance in the same arbitrary units as the initial slope e. The quotient e/c would then be a measure of the rate of aqueous exchange, showing directly how large a fraction of the test substance is exchanged per unit of time. It is possible that the amount of radiation coming from the substance of the cornea will no longer be negligible when the aqueous equilibrium is reached. This would hamper the application of the method to human eyes, if no method is found for isolating the corneal radiation. In animal experiments, the activity of the cornea could be determined separately after removal.

The author is engaged in the construction of equipment necessary for experiments along these lines.

of the carotid closure has not been studied as extensively under Numal as in the unanaesthetized state, because it is much more difficult to tonometrize under Numal. The rabbits often develop considerable nystagmus and with our standardized technique, the flaccid animals are more difficult to handle. Enough measurements have been made, however, to allow the statement that on an average carotid occlusion gives about the same pressure drop under Numal as in the unanaesthetized state. The normal intra-ocular pressure is about 5 mm Hg lower under Numal.

The equilibrium concentration of $Na^{(24)}$ in the aqueous after carotid occlusion was determined in 12 rabbits. One common carotid was ligated and an intra-peritoneal injection of $Na^{(24)}$ given within 2 hours afterwards. After about 15 hours, an ample time for equilibration, samples of aqueous were drawn from both eyes and the activity of the samples determined with a conventional counter arrangement, with a capacity well above the activity of the samples. At least 2-3000 impulses were counted, the counting error thus is about 2 per cent. Tonometry of the eyes was not performed in order to avoid every trauma.

Some of the animals which had received Numal intra-peritoneally needed a few supplementary drops of ether and were moreover given one drop of 0·4 Diocain Ciba topically immediately before the paracentesis. Details of technique have been described elsewhere (Bárány 1947*c*). The last animal in the intra-peritoneal group died a few minutes before the aqueous was aspirated. It is included in the table all the same, since there is little reason to expect the equilibrium to change during the first minutes after cessation of breathing.

The result is summarized in table I.

The table shows that there was almost no difference between the sodium content of the aqueous on the side of the closed carotid and that of the control eye. The mean ratio is 0·99. The kind of anaesthesia obviously played no rôle.

There seems to be only one systematic source of error which could play a part in this result, namely contamination of the aqueous with plasma. It is well known that the reduction in intra-ocular pressure caused by a corneal puncture leads to a capillary dilatation and the formation of plasmoid aqueous. When drawing aqueous samples one tries to avoid contamination with newly formed plasmoid aqueous by avoiding contact with the iris, by not emptying the anterior chamber completely, by using only very gentle aspiration and by working quickly. All the same, some slight admixture of plasma might easily occur. We know that at equilibrium in the normal eye, the sodium concentration in the aqueous is about 90 per cent. of that in the plasma. Assume that the aqueous withdrawn from a normal eye is contaminated with 10 per cent. of plasma. A simple calculation shows that this will increase the sodium content of the aqueous by 1 per cent.

TABLE I

The influence of unilateral carotid occlusion on the equilibrium concentration of radiosodium in the aqueous humour.

All activities are corrected for radio-active decay. They have been made comparable by multiplication by the body weight of the animal, because all animals received the same dose of radiosodium. The blood pressures were obtained by means of an ear capsule about 24 hours after the withdrawal of aqueous and about 40 hours after ligation of the carotid.

Animal N:r	Body weight kgm.	Aqueous, counts per minute per 0·1 ml, multiplied with body weight			Mean blood pressure, $\frac{\text{Occluded}}{\text{Control}}$	Anaesthesia, Numal ml/kgm
		Occluded	Control	$\frac{\text{Occluded}}{\text{Control}}$		
10	2·0	766	790	0·97	0·49	0·6 i.v.
12	1·9	1010	1065	0·95	0·53	0·6 i.v.
13	2·0	915	928	0·99	0·48	0·6 i.v.
14	2·1	767	734	1·04	0·57	0·6 i.v.
15	2·1	820	835	0·97	0·60	0·6 i.v.
16	1·7	795	843	0·94	0·43	0·6 i.v.
18	2·3	798	829	0·96	0·71	0·65 i.p.
19	1·9	880	911	0·97	0·48	0·65 i.p. +0·15 i.v.
20	2·2	959	943	1·02	0·69	0·65 i.p.
21	2·1	890	870	1·01	0·48	0·65 i.p.
23	2·5	790	809	0·98	0·56	0·65 i.p.
24	2·5	848	815	1·04	dead	0·65 i.p.
				0·987	0·547	

Now, as is well known (Wessely 1908), plasmoid aqueous is less easily formed on the side of the closed carotid, where the blood pressure is much lower. Therefore, on an average this source of error will tend to increase the sodium concentration predominantly in the control eye. Some part of the slight difference between

experimental eye and control eye found might depend on this source of error.

This result, that carotid occlusion hardly or not at all changes the equilibrium concentration of sodium in the aqueous is in excellent agreement with similar experiments previously made concerning the total osmotic pressure of the aqueous (Bárány 1946*b*, 1947*d*). In 29 experiments on 22 animals, using the Hill-Baldes' thermo-electric vapour tension method, it was found that carotid occlusion changes the osmotic pressure of the aqueous by less than a fraction of one per cent. As sodium chloride is responsible for the absolutely dominant part of the osmotic pressure of the aqueous, the result can hardly imply anything other than that carotid occlusion does not change the sodium chloride concentration.

Thus we have found that in equ. (1) $C_1 \cong C_0$. But then the expression degenerates into

$$\frac{F_1}{F_0} \simeq \frac{E_1}{E_0}$$

It is interesting to note that, because $C_1 = C_0$, the same relation would hold even if sodium had entered by diffusion instead of secretion.

Thus, the constancy of the sodium concentration shows that the relative change in aqueous outflow caused by carotid closure must be very nearly equal to the relative change in rate of entrance of sodium.

How large, then, is the change in rate of entrance of sodium caused by carotid occlusion? With the aid of the result just arrived at, this can be deduced from previous measurements by the author, made for a different purpose (Bárány 1946*c*, 1947*c*).

In these experiments, Na (24) in the form of 5 ml. of normal saline was injected into rabbits intra-peritoneally. One carotid of *the animals had been closed a few hours earlier. After 40-60* minutes, aqueous samples were withdrawn and the activities measured. At this stage, the Na (24) content of the aqueous is still far below that of the plasma. The figures obtained would therefore be almost direct measures of the rates of entrance of Na if the rate of aqueous outflow had been constant. *But, as carotid occlusion reduces the* intra-ocular pressure and the rate of aqueous drainage, any reduction *in rate of entrance caused by carotid occlusion will be partly* compensated for by the concomitant reduction in aqueous drainage. *Consequently, a correction factor has to be applied. This can be* derived as follows:

The experiments were made under the same conditions as those of Kinsey, Grant, Cogan, Livingood and Curtis (1942) on which the theoretical treatment of Kinsey *and Grant (1942) is based. Therefore, equ. (10) of these latter authors which fits* their sodium data should be applicable to ours too. The equation is

$$c_2 = k_2 \cdot c \left\{ \frac{1}{k'} \left(1 - e^{\frac{-k't_1}{V}} \right) - \frac{1}{k_1 V - k'} \left(e^{\frac{-k't_1}{V}} - e^{-k_1 t_1} \right) \right\}$$

Here, c_2 is the radio-sodium concentration in the aqueous,
c the equilibrium concentration in the plasma,
k_2 the co-efficient of rate of entrance,
k' the co-efficient of rate of exit by aqueous flow,
$1/k_1$ the time constant of the equilibration process between the intra-peritoneal depot and the blood,
t_1 the time after intra-peritoneal injection of the sodium salt,
V the volume of the anterior chamber.

The numerical values of the constants are as follows: k' was found by Kinsey and Grant to be about 4 mm.^{3} per minute in the normal rabbit's eye, V is about 250 mm.^{3} and t_1 in our experiments was about 50 minutes. For k_1 we can get a value from the plasma concentration curves of Kinsey *et al.*, which show full concentration after 20-30 minutes. This time thus is about 3 time constants long and k_1 consequently is about 0·1-0·2.

Now, what we want to know is how a proportionally equal reduction in the rates of entrance k_2 and of exit k' influences the concentration c_2 as compared with the other eye of the same animal where k_2 and k' are uncharged.

If the above numerical values are inserted and the expression is evaluated by series expansion including the fourth order terms the following figures are obtained:

Reduction of rates k_2 and k' in per cent. of the normal	10	20
Reduction of concentration c_2 in per cent. of the normal	7·3	15

This result is obtained with $k_1 = 0{\cdot}1$. If the upper limit $k_1 = 0{\cdot}2$ is used instead, the figures become 7·0 and 14·5. On the other hand, if the fifth-order terms are included, the figures increase by a few tenths of one per cent.

The result of the calculations shows, that under our conditions of experiment, the relative reduction in the rate of entrance of sodium is reflected in the scale of 3:4 in the reduction in concentration 50 minutes after the injection. This knowledge allows us to make use of the concentration ratios between experimental eye and control eye obtained in the previous study. These ratios were

0·71, 0·92, 0·93, 0·93, 0·96, 0·98, 1·03, 1·22

The extreme values are without doubt the result of contamination with plasma, which in these experiments had an activity at least twice as high as the aqueous. The mean ratio is 0·96 and the median 0·95. The reduction in concentration caused by carotid clamping is thus about 5 per cent. or probably less because of the systematic error discussed before. Applying the correction factor to this value, we find the reduction in rate of entrance of sodium to be about 7 per cent. And now we have the answer to our problem, because in view of the constancy of the equilibrium concentration, this figure must also very nearly represent the reduction in aqueous outflow caused by carotid occlusion.

The remarkable thing about this figure (7 per cent.) is that it is so small. Even if various errors of estimation have co-operated to give too small a value, this result certainly does not support the idea of an overflow mechanism in the intact rabbit's eye. An intra-ocular pressure drop of 10-15 per cent. should have given a much more

pronounced reduction in aqueous outflow if an overflow mechanism had really existed. The discrepancy is even more striking if one considers the reduction in driving hydrostatic pressure head instead of intra-ocular pressure. According to Seidel (1923), the pressure in the episcleral veins is about 9 mm. Hg in the rabbit. Thus, the hydrostatic pressure in the aqueous drainage channels cannot be less than, say, 10 mm. Hg. The pressure head for aqueous outflow is thus certainly less than 20 mm. Hg in the normal eye and carotid closure causes a reduction amounting to certainly more than 20 per cent. Still there is only a small reduction in aqueous outflow.

III.—Theoretical part

A discrepancy of the magnitude found between the change in aqueous flow and in the pressure head must have an explanation. There seem to be two possibilities.

The first is that in our experiments, the rate of aqueous outflow was influenced, not only by the change in intra-ocular pressure but also by the change in arterial blood pressure as such. If the pressure in the drainage channels were directly dependent on the arterial blood pressure to any appreciable degree, a reduction in arterial pressure could conceivably increase the pressure head between the anterior chamber and the drainage channels and thus partly compensate for the reduction in intra-ocular pressure. It seems improbable, however, that this mechanism is very important. The drainage channels are venous vessels, the pressure of which is only dependent to a very slight extent on the arterial blood pressure. In so far as there is a small dependence, however, this mechanism could explain part of the discrepancy.

The other and more probable explanation is that the force which causes the outflow of aqueous consists of two parts, one of them a hydrostatic part which changes directly with the intra-ocular pressure and the other one an osmotic part, which is more or less constant.

The idea that osmotic forces play a part in the mechanism of Schlemm's canal originates from Friedenwald and Pierce (1932). Troncoso (1942) assumes that the drainage vessels of the sub-primate eyes, the trabecular veins, contain flowing blood which osmotically attracts aqueous humour. In animals, Friedenwald and Scholz (quoted Friedenwald 1940, 1942) have demonstrated "plasma and some red blood cells in the vessels which formed the base of the sclero-corneal trabeculum" after freezing the anterior segment of the eye with liquid air. The present findings indicate the existence of a constant absorptive force besides the changing hydrostatic one. There is thus every reason to consider how the mechanism of aqueous drainage will behave if the movement of the aqueous is the result of a combination of the two forces working in the same direction. The

histological findings of Friedenwald and Scholz indicate that attention should be given to the possibility of a considerable dilution of the plasma in the relevant vessels.

The veins of the filtering angle, which are supported by scleral strands, are, as far as the author is aware, the only minute vessels of the body which need not collapse as soon as the external pressure exceeds the internal. Consequently, in these vessels, the osmotic pull of the plasma colloids and the hydrostatic push can co-operate. This fact allows higher driving forces for fluid absorption than elsewhere and dilution of the streaming plasma by absorbed fluid should consequently more easily become evident.

Consider such a vessel. If it were completely filled with blood, the situation would be simple. The driving force behind the passage of aqueous humour would then be the sum of the hydrostatic pressure difference and the colloid-osmotic attraction of the blood plasma. However, the blood in the vessel is not pure: it becomes more or less diluted by aqueous humour when it absorbs the efflux from the anterior chamber. This reduces the osmotic attraction along the path of the blood through the vessel. When the intra-ocular pressure rises and more aqueous humour is forced out hydrostatically, this dilution will become greater and the colloid-osmotic attraction consequently smaller. When the intra-ocular pressure falls, the blood in the vessel becomes less diluted, and the colloid-osmotic attraction for aqueous humour rises. Plainly, we have here a mechanism that tends to keep the flow of aqueous humour constant, the direct opposite of an overflow mechanism. The degree of constancy achieved is clearly dependent on the rate of the blood stream through the vessel. When there is no blood supply at all, the colloid-osmotic factor disappears. The rate of efflux of the aqueous humour will then be in direct and simple proportion to the hydrostatic factor; there will be no stabilization of aqueous flow. When there is a very rapid flow of blood, the converse will be found—*i.e.*, a constant and fairly high osmotic attraction, which admittedly reduces the relative importance of the variable hydrostatic factor, but on the other hand does not stabilize the flow of aqueous absolutely. The stabilization tendency only appears in intermediate cases, but here the quantitative relations become so complicated that they cannot be treated in words. I have therefore made a mathematical calculation of how the fluid exchange over a vessel wall behaves, taking into account the change of the colloid-osmotic pressure which the plasma undergoes when it flows through the vessel.

I have not been able to find any previous treatment of this problem, which is one of general physiological interest. This may possibly be because the general case of the problem leads to a differential equation which cannot be solved exactly. The difficulty arises if one tries to pay regard both to the osmotic conditions varying along the

vessel, and to the variations in the hydrostatic lateral pressure along its course. As we are dealing with a venous vessel with relatively large surface and cross section a first approximation can ignore the differences in lateral pressure which may exist between different parts of the vessel: these can only be very small in relation to the other active forces. We therefore assume that there is the same hydrostatic pressure in the whole vessel as far as this comes into contact with the aqueous humour.

Thus, we consider a linear vessel, through which blood flows. The lateral pressure in the vessel is everywhere equal to p_v. The colloid-osmotic pressure p_o is a function $p_o(l)$ of the position l. On entering the vessel $p_o = \bar{p}_o$. Outside the vessel there is aqueous humour under the intra-ocular pressure of p_i. (It is in relation to the aqueous humour that the colloids have the osmotic pressure of p_o — by this definition, we avoid most of the complications that might arise from considerations of Donnan effects). The blood streams into the vessel with the volume rate of V_i for plasma. During its passage through the vessel it takes up a certain volume of aqueous humour, partly by osmotic attraction and partly by hydrostatic filtration. The volume absorbed per unit of length and time, the specific absorption rate, will be called a. It is a function of l. The quantity absorbed in the vessel up to a point l is called A. We then have

$$A = \int_0^l a\,dl \text{ and } a = \frac{dA}{dl}$$

At the point l, the plasma has already been diluted to a certain degree. If there has been complete mixture, the degree of dilution is $V_i/(V_i+A)$. The diluted plasma has a lower colloid-osmotic pressure. We will assume for the sake of simplicity that the pressure is proportional to the concentration. This is not strictly so, and we shall be discussing what the simplification implies. On this assumption, however, the colloid-osmotic pressure at the point l will be

$$p_o = \bar{p}_o \cdot \frac{V_i}{V_i+A}$$

The hydrostatic pressure head is everywhere $p_i - p_v$.

Let us express the hydrostatic driving force in terms of the colloid-osmotic pressure of the undiluted plasma, $\bar{p}_o$ and define a relative hydrostatic pressure γ as

$$\gamma = \frac{p_i - p_v}{\bar{p}_o}$$

In the normal eye, γ cannot be much larger than about 1·0 or much less than 0.

The specific absorption rate $a = \frac{dA}{dl}$ is the product of the driving force and the specific filtration capacity of the vascular wall, g, at the point l:

$$a = \frac{dA}{dl} = g\left(\bar{p}_o \cdot \gamma + \bar{p}_o \cdot \frac{V_i}{V_i + A}\right)$$

The integration of this differential equation using the boundary conditions ($l=o$, $A=o$), gives

$$\bar{p}_o \int_0^l g\,dl = \frac{1}{\gamma^2}\left[\gamma A - V_i \ln\left(1 + \frac{A}{V_i} \cdot \frac{\gamma}{1+\gamma}\right)\right]$$

On the left we have the absorption rate for aqueous humour which the vessel would have had for purely osmotic reasons if it had been filled with pure plasma. We will call it O. We express the true absorption A and the plasma flow V_i in O as unit.

$$A = a \cdot O;\ V_i = v_i \cdot O$$

Insertion of this and rearrangement finally gives the relation sought, even if only implicitly, between relative absorption rate, a, and relative hydrostatic pressure, γ. As parameter we have v_i, the relative plasma flow:

$$a = \gamma + \frac{v_i}{\gamma} \cdot \ln\left(1 + \frac{a}{v_i} \cdot \frac{\gamma}{1+\gamma}\right)$$

For $\gamma=0$ this expression is indefinite. The limiting value, however, is:

$$a_o = \sqrt{v_i^2 + 2v_i} - v_i$$

The equation cannot be evaluated exactly for other values of γ. Fig. 1 shows a number of solutions for different parameter values, obtained by graphic and numerical approximation. This has been taken to a point where the errors of the single ordinates do not exceed some few per cent.

The result of taking plasma dilution into consideration is visible in two properties of the graphs of Fig. 1.

First, the whole level of the curves, inclusive of the intersection with the ordinate axis, is dependent on the rate of plasma flow, v_i. Without plasma dilution, they would all start at $a=1{\cdot}0$ for $\gamma=0$. Secondly, the slope of the curves is smaller than 1·0 and especially small in certain pressure regions, where an inflection occurs. If there were no plasma dilution, the slope would have been 1·0 everywhere. This now only is the case for $v_i=0$ and ∞.

The smallest slope is found at the initial part of the curve for the smallest plasma flow, $v_i=0{\cdot}01$. Here, consequently, the highest degree of absolute stabilisation of aqueous flow by the "dilution mechanism" occurs. The slope is only 0·7 and is even less for

negative γ and smaller v_i. With higher rates of plasma flow, the corresponding region, which is visible in the higher curves as a small inflection, is displaced towards higher γ values and become less and less important.

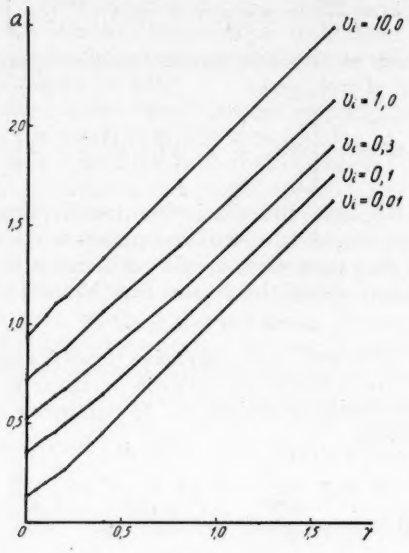

FIG. 1.

The rate of fluid absorption by a vessel under combined osmotic and hydrostatic influence.

Abscissae: γ = relative hydrostatic pressure head.
Ordinatae: a = relative rate of fluid absorption.
Parameter: v_i = relative rate of plasma flow through the vessel.

For $\gamma > 0$, the osmotic and hydrostatic forces co-operate, for $\gamma < 0$ they oppose each other. All the curves intersect at $a = 0$, $\gamma = -1{\cdot}0$. Consequently the slope gradually decreases towards the left. The curve for $v_i = 0{\cdot}001$ is steeper than that for $v_i = 0{\cdot}01$ in the interval shown.

In Fig. 1 the reduction of slope caused by the "dilution effect" appears not to be very important except in restricted regions and at low rates of plasma flow. However, in the derivation of our formula we have neglected certain factors which certainly will increase the "dilution effect" considerably.

First of all, we have assumed that the colloid-osmotic pressure sinks in proportion to the degree of dilution of plasma. As a matter of fact, it sinks considerably more (see Meyer 1932 for references and discussion). This naturally increases the dilution effect.

Furthermore, we have assumed that complete mixing between plasma and aqueous takes place in the vessel. This is not quite impossible, but on the other hand it is very probable that a certain

degree of stratification occurs at higher rates of aqueous flow, so that the fluid actually in contact with the vessel's wall is more dilute than the bulk of the fluid. This would be in agreement with the observations of Ascher and Goldman on man, where stratification of the blood and aqueous in episcleral vessels has been directly observed. A mechanism of this kind would materially increase the "dilution effect."

Finally and this is probably the most important point, we have treated only one vessel. Let us consider the situation if there are several vessels connected "in parallel" in the electrical sense, at varying depth in the sclera. A considerable influx of aqueous into those who are most accessible will deflect the blood stream into other vessels which have less contact with the aqueous. The plasma in the most accessible vessels will then be even more diluted than in our calculations, with a corresponding reduction in osmotic pull and a tendency towards absolute stabilisation of the rate of aqueous flow.

Until now, we have discussed the matter with regard to the absolute amount of aqueous flow and the stabilisation of this absolute amount. With respect to the regulation of the intra-ocular pressure, however, the relative variations of aqueous flow with changing intra-ocular pressure are more important. Summarizing the situation from this point of view we find the following:

(*a*) If the plasma flow through the trabecular veins is considerable, there is possibly not much absolute stabilisation of aqueous flow but instead a considerable "basal" flow even at zero hydrostatic pressure head. This results in a considerable relative stability of aqueous flow in spite of changing intra-ocular pressure.

(*b*) If the plasma flow through the trabecular veins is small, there probably is only a small "basal" flow at zero pressure head but instead a considerable absolute stabilization of aqueous flow. This also results in a considerable relative stability of aqueous flow in spite of changing intra-ocular pressure.

Thus we find that the existence of an osmotic factor in the aqueous outflow mechanism reduces the efficiency of the drainage mechanism in its rôle as a stabilizer of intra-ocular pressure in several ways. The osmotic factor both absolutely and relatively reduces the rate of change of aqueous flow with pressure, it tends to keep up a constant flow of aqueous.

The theory given thus explains the experimental findings presented in the previous section at least qualitatively. Moreover, it is in excellent agreement with some findings by Friedenwald and Pierce (1932). These authors observed, that if the rate of inflow of saline into a dog's eye is plotted as a function of pressure, the curve shows a definite inflection where the increase in flow per unit pressure increase is much smaller than at higher and lower pressures. Some of their results are reproduced in fig. 2. There can hardly be any

doubt that this behaviour of the curve is due to the plasma dilution mechanism discussed above.

In the experiments of Friedenwald and Pierce, the normal intra-ocular pressure is stated to have been 3-10 mm. Hg below the beginning of the inflected region. A pressure drop of this magnitude could easily be caused by the general anaesthesia. Moreover, the intra-scleral venous pressure could have been higher during anaesthesia. It seems not impossible, therefore, that in the unanaesthetized

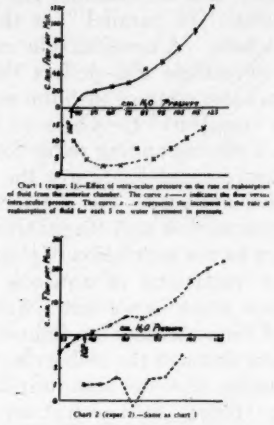

FIG. 2.

The rate of inflow of saline into the eyes of anaesthetized dogs. From Friedenwald and Pierce (1932).

dogs, the intra-ocular pressure was high enough to allow the drainage mechanism to operate in the inflected region, where aqueous flow is stabilized. The results obtained above for the normal rabbit's eye may perhaps indicate that this holds for the rabbit too.

How the situation is in man remains to be seen. The results of this study are not directly applicable to man, who has no trabecular veins. Friedenwald (1936) has made it seem very probable that the aqueous in the canal of Schlemm is mixed with a certain amount of plasma derived from special arterial connections. On principle, therefore, a similar kind of dilution mechanism could very well operate in the canal of Schlemm too, keeping the flow of aqueous more or less constant and decreasing the pressure - stabilizing properties of the drainage mechanism.

IV.—Concluding remarks

We have now arrived at the end of this investigation. Starting with the expectation of finding properties of the aqueous drainage mechanism which might be useful in stabilizing the intra-ocular

pressure, we have arrived at quite the contrary result. Experimental as well as theoretical findings point to the existence of a mechanism which, far from being suitable for stabilizing the intra-ocular pressure, is suitable for stabilizing the rate of flow of aqueous instead. What kind of physiological function could such a mechanism fulfil?

The answer lies near at hand if we once stop to consider the aqueous as merely something that causes intra-ocular pressure. The aqueous is the blood of the lens. What we have stumbled upon is a mechanism by means of which a fairly constant circulation of aqueous could be maintained in spite of the changing intra-ocular pressure.

In the "architecture of bodily function," a hierarchy of regulations exists. We have a regulation of blood pressure by the baroceptors, but this regulation is subordinated to the need for adequate blood flow through vital and working organs. In case of conflicting purposes, the blood pressure regulation just gives in.

This simile may be extended to the eye. There is possibly a regulation of the intra-ocular pressure to which the drainage mechanism could possibly contribute. But this regulation seems to be subordinated to the need for a constant aqueous flow, which gives the lens a constant environment. In the cataracts which accompany various disturbances of intra-ocular pressure and aqueous flow we see what may perhaps be the result of overtaxing this mechanism. In fact, it is tempting to go even further: might not the glaucomatous pressure rise be considered, at least in some cases, as an adaptation, securing an adequate circulation of aqueous in face of impaired drainage facilities?

Summary

1. A new method of studying the dependence of aqueous outflow on intra-ocular pressure in the completely intact eye is described and applied to the rabbit. It is based on determinations in the aqueous of equilibrium concentration and rate of entrance of a substance at different levels of intra-ocular pressure.

2. Unilateral carotid occlusion does not change the equilibrium concentration of radiosodium. This shows that the change in aqueous outflow caused by the operation and the concomitant eye pressure drop is proportionally equal to the change in rate of entrance of radiosodium into the aqueous humour.

3. Unilateral carotid occlusion reduces the rate of entrance of radiosodium into the aqueous humour by only about 7 per cent., probably somewhat less. This shows that the reduction in aqueous outflow is percentually smaller than the reduction in intra-ocular pressure and hydrostatic pressure head. Thus, there must be some kind of relative stabilization of the rate of aqueous flow.

4. The influence of the hydrostatic driving force would be less if osmotic forces participated in the aqueous drainage mechanism.

Mathematical treatment of fluid absorption by a vessel under combined osmotic and hydrostatic action shows that if the diluting effect of the absorbed fluid is not insignificant, a certain absolute as well as relative stability of fluid absorption will obtain, in spite of changes in the hydrostatic pressure relations.

5. The results indicate the existence of an aqueous drainage mechanism which tends to keep the rate of aqueous flow constant even at the expense of the stability of the intra-ocular pressure. Such a mechanism could be significant from the point of view of the lens.

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A CASE OF BILATERAL GENUINE IRIS-ATROPHY*†

BY

IDA CYUKRÁSZ, M.D.

A lady, aged 24 years, came to the clinic complaining of intolerable headache and bad vision of the right eye. The left eye was always blind. Clinical findings: sight of right eye finger counting 1 metre,—8·0 D =1/3 : left, no light perception. Pressure on both sides 56 Hg mm. Right eye: eccentric pupil directed to 3 o'clock, roughly triangular in shape reaching almost to the iris-root. Pigment border nasally below and above is intact. Iris tissue very atrophic, the iris-frill can be seen only above and below. Temporally

* Received for publication, November 15, 1946.

† Report from the Univ. Eye Clinic Debrecen. Leader: Prof. Kettesy.

there is a big defect from 8-11 o'clock extending to the angle of the anterior chamber. Between the hole and the pupil a 5 mm. iris strip is left with lack of iris-frill and pigment border. The defect is bridged over by two fibres of iris tissue. Some part of the posterior pigment layer of the iris is adherent to the lens-capsule. The lens is transparent, vitreous normal and so is the cornea. On the fundus there is a venous pulse and deep glaucomatous excavation. Visual field on the right side contracted, only a quadrant remains in the upper internal area (Fig. 1). Left eye: corneal surface slightly stippled. The pupil is continued to 12 o'clock in a congenital coloboma but there is no defect in the ciliary body nor in the choroid. Iris tissue atrophic, pigment border continuous with the angle of the anterior chamber but reduced, the iris-frill is well shown. Two

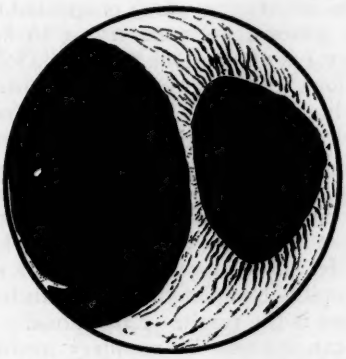

FIG. 1.

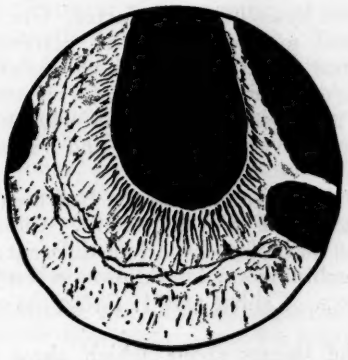

FIG. 2.

holes can be seen in the region of the iris-root one at 11 o'clock, the other from 1-4 o'clock that includes all the layers of the iris. The greater defect is divided in two by a stout bundle of trabeculae. There is a slight iridodonesis, the lens and the vitreous are normal and in the atrophic disc is a deep glaucomatous excavation (Fig. 2).

Regarding these findings, we could find neither macroscopic, nor slit-lamp evidence of previous inflammation in the left iris—an atypical coloboma is seen. We made the diagnosis of genuine iris-atrophy.

The genuine or essential iris atrophy is a well known but rare disease. In the University Eye Clinic, Debrecen, we have seen only two cases during the last 25 years. The first was published by Prof. Kettesy (Kreiker) in 1923. He observed the alteration in a lady aged 41 years, the other patient was a man aged 40 years, in whom there was a bilateral iris atrophy which progressed to total aniridia.

Regarding the genesis we were trying to find some solution. Clinical and laboratory examinations were made for tuberculosis, lues, endocrine aberrations without any positive result.

Reports in the literature show in some cases that hyper-sensibility of the thyroid and suprarenal glands could be proved, but this had no importance in the prognosis and absolute glaucoma.

As far as we can see, an explanation of this rare disease can be given only by the embryological dynamics, by that regressive power which is able to set in motion the pupillary evolution in the fourth month of foetal life. The process finishes soon enough, sometimes even before the pupil is completed. When this happens a persistent pupillary membrane is the result. Exceptionally a trauma or some other influence can regress the pupillary membrane during life also. Kreiker's published case is a nice example, and Wolfrum's experiments seem to be able to prove this assumption too.

We come to the conclusion that the regressive function of the iris is influenced by an inhibitory factor. One can imagine, if in these embryological mechanics, in the activity of action and reaction, the faintest disturbance arises, the balance overturns, and develops, what Riger called, the dysgenesis mesodermalis.

No doubt, the solution of the question will be given by getting more insight into the embryological and respectively biological happenings.

From the practical point of view, the treatment of the secondary glaucoma seems to be the most important. Ciotola, Licskó, de la Vega, Post, Barkan and others have done different anti-glaucomatous operations. Trephining and irido-sclerectomy are the most frequent operations. Csillag and I. Grósz do cyclodialysis with good results.

If we take the figures above, which show the huge defects in the iris the decision of cyclodialysis is obvious. There

is only one question, where to make the operation, which part of the ciliary body shall we detach? We decided, referring to the intact part of the iris, at the insertion of the inferior rectus muscles. Next day the pressure was subnormal (12 Hg mm.) and for half a year there has been no alteration in the pressure.

As far as we are concerned we would propose in cases of genuine iris-atrophy combined with high pressure a cyclodialysis a tergo (secundum Blaskovics) at the insertion of inferior rectus muscle.

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THE DEVELOPMENT OF MEDICAL STUDIES IN BRITAIN: OPHTHALMOLOGY*

BY

R. R. JAMES

Earliest Times

ENGLISH ophthalmological history may be said to start with the Roman occupation of Britain. From the large number of oculists' stamps which have been unearthed on Roman sites we know that a good deal of local treatment of eye conditions by way of collyria and ointments was practised at this early date. After the withdrawal of the legions there is a long gap in our knowledge; in fact nothing is known until we come to the Anglo-Saxon *Leech* [medical] books and Herbals. Here again, treatment was mainly by local applications of infusions of herbs and the secretions of animals, such as gall mixed with honey, and even of human urine. Charms also played a large part and we may say that Anglo-Saxon ophthalmology has every appearance of having been largely futile.

The Norman Conquest and after

The Norman Conquest did little to improve the practice of ophthalmology but the 13th century saw the beginnings of optics

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in Britain. Grosseteste, Bishop of Lincoln, was the teacher of Roger Bacon (died 1294), who proved that spherical *plus* spheres would be of use for reading in old people; while John of Peckham (died 1294), later Archbishop of Canterbury, is credited with the discovery of the use of concave refracting surfaces, and his *Perspectiva Communis* was for the next few centuries the only text-book on optics to be used in England.

In the year 1377 John of Arderne wrote his little book entitled *De cura oculorum,* of which manuscripts in Latin and in 15th-century English exist among the *Sloane Manuscripts* at the British Museum, and in the Library of Emmanuel College, Cambridge. This booklet is a mere compilation of other people's views, much of it being taken from Lanfranc. English ophthalmology had, in fact, made very little progress since Anglo-Saxon times.

The Sixteenth and Seventeenth Centuries

The closing years of the 16th century saw the publication of two small books dealing with ophthalmology. One was Walter Bayley's *Briefe Treatise Touching the Preservation of the Eye-sighte,* and the other a translation (probably by A. Hunton, of Newark-on-Trent) of Guillemeau's *Maladies de l'Œil.*

Early in the 17th century Richard Banister, of Stamford, brought out a duodecimo of 478 pages containing five separate treatises. Of these the first 112 pages are Banister's own contribution, and this section is named Banister's Breviary. Though he was an itinerant oculist it is obvious that Banister was a much more honest practitioner than the rest of his ophthalmic contemporaries. He it was who first pointed out the cardinal sign of hardness of the eye-ball in cases of *gutta serena,* in this case glaucoma. The significance of his observation was not recognised, and raised intra-ocular tension was forgotten for the next 150 years. Banister was also almost certainly the author of the manuscript in the British Museum (*Sloane Manuscript,* 3801) which throws much light on the manners and customs of the itinerant charlatans of this date. Several of these are named, such as Luke of Erith, Mr. Surphlete of King's Lynn, and Henry Blackborne. The last-named is severely criticised by Banister, and it is a sign of the looseness of the times that Blackborne in 1605 received the Archbishop of Canterbury's licence to practise in diseases of the eyes. Richard Banister must have been a remarkable man and has deserved well of ophthalmology.

Turberville of Salisbury (died 1696) was a qualified medical man in an age of unqualified quacks. He had a large practice and made a valuable contribution to ophthalmology in extracting an iron particle from the cornea with a magnet. Another qualified English physician of this time was William Briggs, who published the

Ophthalmographia and the *Nova Visionis Theoria*. He described the papilla of the optic nerve in 1676 and, in 1684, recorded in the *Philosophical Transactions of the Royal Society* a case of night-blindness. Dimness of vision following the administration of Peruvian bark in fever was described in 1681 by a general practitioner at King's Lynn in a letter to Briggs.

The Eighteenth Century: Charlatinism and the Foundations of Modern Ophthalmology

The 18th century was the age of ophthalmic quackery, but it saw the foundations of modern ophthalmology laid by such masters as Cheselden, Sharp and Warner. Cheselden devised the operation of iridotomy in the making of an artificial pupil, and Sharp and Warner perfected the operation of extraction of cataract, a great advance on the age-long method of couching [displacement of the cataract from the visual axis].

Duddell, a pupil of Woolhouse, wrote a good account of diseases of the cornea in 1729. Later in the century, James Ware wrote on syphilis in connexion with ophthalmia, and brought some order out of chaos in the matter of conjunctival diseases. Gataker wrote on the anatomy of the eye and on the use of belladonna, and Wells on double vision.

The chief 18th-century ophthalmic quacks were William Read, Roger Grant, and the Chevalier Taylor. Read and Grant were illiterate; the former was knighted by Queen Anne. The Chevalier Taylor was quite a remarkable person. In professional knowledge he was often far ahead of his time, but he practised all the arts of unblushing effrontery and charlatanism. He was oculist to George II, and his son and grandson followed in his footsteps though they were not of the same calibre. Eighteenth-century Royalty was singularly unfortunate in its oculists, as George Coats pointed out.

The end of the century, in 1794, saw the publication by John Dalton of the history of his colour blindness. Thus, it will be seen that up to the end of the 18th century ophthalmology had not advanced very far, but better times were to come.

Rational Ophthalmology displaces Charlatanism

The year 1805 saw the foundation of *Moorfields Eye Hospital by J. C. Saunders, and this more than anything else struck the death blow to the quackery of the previous century. Provincial Eye Hospitals were founded at Exeter in 1808, Bristol in 1810, and Manchester in 1814. The Royal Westminster Ophthalmic Hospital was founded by Guthrie in 1816, the Central London

* Now the Royal London Ophthalmic Hospital.

Ophthalmic Hospital in 1843, the Western Ophthalmic Hospital in 1856 and the Royal Eye Hospital in the year following. The first course of lectures on diseases of the eye was given by Guthrie at the Royal Westminster Ophthalmic Hospital.

An earlier epoch-making date in ophthalmological history is 1801, when Thomas Young published his paper on the mechanism of the human eye in the *Philosophical Transactions*. He described astigmatism and measured the amount of the astigmatism in his own eye. His table of optical constants has been only very slightly modified by modern research. His theory of colour vision postulated the presence in the retina of three " fibres," which correspond to the colours red, green and violet respectively. This theory was later resuscitated by Helmholtz and is known as the Young-Helmholtz theory. Young's experiments on interference strongly supported the undulatory theory of light already adumbrated by Sir Isaac Newton and Huygens.

Ophthalmological Literature and Societies

The first real text-books of ophthalmology in Britain belong to the first half of this century. In 1830 William Mackenzie of Glasgow brought out his great work on diseases of the eye. It was far ahead of any previous text-book on the subject and it ran to a fourth edition. Mackenzie was a master clinician, and was the first surgeon to give an adequate account of sympathetic ophthalmitis. Sir William Lawrence's text-book appeared in 1833, and Richard Middlemore's in 1835. Before this, Travers had brought out his synopsis of diseases of the eye in 1820. It ran to a third edition. J. C. Saunders published a book before his untimely death, and did much to revolutionise the treatment of congenital cataract by insisting on early discission. In this he followed the practice of Woolhouse, an English surgeon, who was resident in Paris for many years in the previous century.

Wardrop's *Essay on the Morbid Anatomy of the Human Eye* laid the foundations of ophthalmic pathology; Tyrrell's *Diseases of the Eye*, in two volumes, appeared in 1840; and Dalrymple's splendid atlas belongs to about this date.

The year 1881 saw the foundation of the *Ophthalmological Society of the United Kingdom* with Sir William Bowman as first president. It grew out of informal discussions in the house-surgeon's room at old Moorfields, and of the Committee appointed to make arrangements for its foundation Sir Thomas Barlow was at the time of his death the last survivor. Sir H. Lindo Ferguson of New Zealand is also still with us as an original member of the Society. The Society now has, as affiliated members, the *Oxford Congress*, founded by R. W. Doyne, the *North of England*

Ophthalmological Society, founded by Percival Hay and J. Gray Clegg, the *Midland and South Western* Societies, the *Irish Ophthalmological Society*, and the *Scottish Ophthalmic Club*. A volume of *Transactions* has been published each year without a break since 1881, and the series forms a rich mine of ophthalmological facts.

In 1857 the staff at Moorfields began the publication of the invaluable *Ophthalmic Hospital Reports*, which ran to 20 volumes. In 1864 J. Z. Laurence and T. Windsor began the publication of the old *Ophthalmic Review*. It came to an untimely end 3½ years later and the new *Review* was started in 1881 by Priestley Smith of Birmingham and Karl Grossmann of Manchester. The *Ophthalmoscope* was founded by Sydney Stephenson in 1903. In 1917 the first number of the *British Journal of Ophthalmology* appeared. It incorporates the *Moorfields' Reports*, the *Ophthalmic Review* and the *Ophthalmoscope*, and has continued without a break to the present day.

Ophthalmic Instruments and Operations

English ophthalmology has been responsible for many inventions of ophthalmic instruments. It should not be forgotten that William Porterfield (died 1771) devised the first optometer. Charles Babbage, in 1848, constructed an ophthalmoscope which left little to be desired. He showed it to Wharton Jones, who, alas! did not realize the importance of the means of research thus placed at his disposal. Babbage was a mathematician, not an ophthalmic surgeon, and finding that Wharton Jones was not interested in his model he took no further steps and it was left to Helmholtz to bring out his instrument in 1851. Tyrrell devised the iris hook which bears his name; Bowman a trephine for the eye-ball; Mules of Manchester first suggested the insertion of a glass globe in the sclerotic after evisceration of the eyeball, and his practice was later modified by Frost and Lang, who inserted globes of glass or metal into the orbit.

Corneo-sclerotic trephining for chronic glaucoma was first proposed by Freeland Fergus of Glasgow in 1909. In the next year Elliot, of Madras, improved the operation by splitting the superficial layers of the cornea in order to make more sure of tapping the anterior chamber, and the operation has been known by his name ever since. Herbert, of the Indian Medical Service, also made important additions to our anti-glaucoma methods at this date.

Stanford Morton's ophthalmoscope was for years the best of its kind, though Frost's instrument was a close second. Frost also brought out an extremely effective model eye for teaching purposes.

Ophthalmology as a Speciality

In the early years of the last century ophthalmology was still, in Britain, a part of General Surgery; Sir William Bowman was the first general surgeon to give up his surgical work at King's College Hospital in order to become a pure ophthalmic specialist. With George Critchett, Bowman was responsible for the foundation of this speciality. But Critchett, and even Jonathan Hutchinson, were general surgeons primarily and ophthalmic surgeons in the second place.

Bowman's name is a household word in ophthalmology. Bowman's membrane, his probes, and " stop " needles are known everywhere; but it was his guiding hand which placed ophthalmology as a speciality on a sure footing. Lawrence wrote on syphilis of the eye. Hutchinson's monograph on syphilitic disease of the eye and ear is a classic, and he was the first to describe the notched incisors in congenital syphilis which will always be known as " Hutchinson's teeth." It is reputed that a French surgeon who visited Moorfields in the early 60's rushed into the out-patient room exclaiming " Where is Monsieur Hutchinson? I want to see his teeth."

Hutchinson's main assistants were Waren Tay and Edward Nettleship. Tay never cared for publicity and was glad to remain in the background. Hutchinson's mantle may be said to have fallen on Nettleship, who had a profound influence in the teaching of ophthalmology in his generation.

Argyll Robertson first described the tabetic pupillary reactions which have ever since borne his name; and in an earlier decade Arthur Jacob, of Dublin, first described the layer of rods and cones in the retina in 1819.

One of the first atlases of the fundus was that of Liebreich who was ophthalmic surgeon to St. Thomas's Hospital. He had been turned out of Paris at the beginning of the Franco-Prussian War of 1870, and came to England. There have been several good atlases since his day, notably that of Frost, the pictures in which are still unsurpassed.

Ophthalmic pathology has been well served by the long line of curators of the museum at Moorfields Hospital. Nettleship, Lawford, Treacher Collins, all made notable contributions in this subject, but George Coats, who died in 1915, probably contributed more papers of lasting value than any other, with the exception of Sir John Parsons whose magnificent *Pathology of the Eye* in four volumes has long been a credit to British ophthalmology.

For many years the importance of the state of the refraction of the eye was overlooked and underestimated. A case of Brudenell Carter's published in the Clinical Society's *Transactions*, in 1875,

was one of the first to call attention to the importance of this branch of work; and partly in consequence a demand arose for hand-books on refraction; among these, that of Hartridge ran through many editions and was deservedly popular.

In the field of medical ophthalmology, the manual by Sir William Gowers was pre-eminent for many years: its third edition was brought out by Marcus Gunn who, from his experience as Ophthalmic Surgeon to the National Hospital, Queen Square, did much to advance ophthalmology in its relations to neurology. Perimeters have been invented by McHardy, by Priestley Smith and by Sir William Lister. Priestley Smith won the Jacksonian prize at the Royal College of Surgeons in 1878 with his essay on glaucoma. Few men have had more influence on their speciality of recent years than this celebrated Birmingham ophthalmologist.

Ophthalmological Education

Postgraduate education in ophthalmology is given at the universities and at all the great eye hospitals in London and the provinces. Courses of lectures which include all ancillary subjects such as optics, operative surgery, bacteriology and pathology are given during the terms, and at the same time the student takes his place as clinical assistant to one or more of the members of the senior staff in the out-patient department. If time is no objection, he is wise to hold the post of House Surgeon for a year or more at one of the Eye Hospitals. Even if he does not, he obtains a thorough grounding in clinical ophthalmology, and it is this aspect of teaching which has produced so many of the great names of British ophthalmology during the past hundred years. Special diplomas notably the D.O. Oxon. (1907) and the D.O.M.S. (1920) are awarded to students who pass the qualifying examinations, and for many years ophthalmology has been one of a number of special subjects which can be taken in the examination of F.R.C.S. (Edinburgh).

Preventive and Social Aspects of Ophthalmology

Steady progress has been made during the present century both in prevention of blindness and in amelioration of the conditions of the blind. Blind pensions are now awarded, and ophthalmic monetary benefits under the National Health Insurance came into force in 1925.

Early in its history the *Ophthalmological Society* appointed a deputation, led by Bowman and Hutchinson, to interview the Home Secretary and draw attention to the ravages caused by *ophthalmia neonatorum*. It was pointed out that this affection is largely preventable, and it was suggested that the Registrar

of Births should hand each person registering a birth a printed paper telling him what to do if the baby's eyes showed any signs of inflammation. No action was taken and little was done by the authorities until the *Metropolitan Asylums Board* established St. Margaret's Hospital in 1918 for the treatment of *ophthalmia neonatorum*, affording facilities for the admission to hospital of both mother and child. The *Board* also did good pioneer work by establishing, in 1903, residential schools for the treatment of trachoma in children, at the same time ensuring the continuance of their education.

The *London County Council*, at the instigation of Mr. James Kerr and Mr. Bishop Harman, made a notable advance by segregating partially-sighted children in special—so-called " myope " —schools. Valuable reports on the prevention of blindness have emanated from Glasgow in 1926 and in 1942, and from the Union of Counties Association for the Blind in 1932; and the Ministry of Health has at last set up a Standing Committee on the Prevention of Blindness.

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ANNOTATIONS

On second opinions

A doctor, in discussing with a friend the foibles of patients in general, is reputed to have said that if he suggested a consultation, it was because he did'nt know what was the matter, and that if he pooh-pooh'd the idea as unnecessary, he was afraid of showing his ignorance. As in a large number of cases it is impossible to be dogmatically sure of one's diagnosis it is a wise plan to have a second opinion; and in many cases a consultation will be of great help in settling the line of treatment to be adopted. An intelligent patient will understand the problem if it is placed before him squarely, and will be willing to pay the necessary fee. In the case of what Shakespeare somewhere calls " a blinking idiot " a second opinion is even more necessary in order to safeguard oneself.

We do not mean to imply that extra advice should be proposed in all cases. As a general rule a straightforward case of cataract ready for operation need not be referred to anyone else. Probably it would be wise in cases of diabetes with cataract to have a consultation, usually with a physician, before undertaking any operation at all.

A second opinion is often called for in cases of the more chronic forms of glaucoma. It should certainly be pressed upon a subject with a wounded eye in view of the possibility of the onset of sympathetic ophthalmitis. Border line cases between our own speciality and others, such as neurology and the nose and throat department should have this extra advice.

Sir William Bowman, in consultation, is said to have spoken shortly, in simple language and to have kept strictly to the point; and this attitude is recommended to those who have to act in this capacity.

The suspicious patient may assume that his doctor and the second opinion are acting in collusion against him, but this cannot be helped.

It is wise, if seeing a patient in his own home, to attend strictly to the business in hand when talking over the matter with the doctor who has called you in. Bearing on this point an aprocryphal story is that a very plain looking lady arranged for her sister to be secreted in an annexe to the dining room so that she could hear and report what the doctors said to each other about the case. When the door was shut the consultant is reputed to have said "what a horribly ugly patient," to which the G.P. replied "my dear Sir, you should see her sister."

On appointment books and appointments

When the writer started in practice most surgeons relied on the appointment books supplied by Burroughs, Wellcome & Co. Their books were excellent, of handy size, well arranged and packed with useful information. They were supplied in two varieties, one for the consultant and the other for the general practitioner. Those who remember the book will recall that the publishers provided a specimen page to show how it should be used. Out-door appointments were to be entered in red ink, appointments at home in black. In our early days we often looked with envy on the specimen page. Appointments started at 9.30 a.m., and most of the spaces were filled up till tea time. The last entry "Dinner, Med. Soc. Speech," always tickled our imagination. Only one hour was allotted to hospital visits, so we presumed that the hypothetical surgeon was not attached to any ophthalmic hospital. This page must have been prepared long before the days when each consultant had a secretary or a part share in one. When did the Victorian surgeon write his letters? Sir James Paget wrote most of his after dinner at night we are told in his life.

We have known elderly ladies being very angry at receiving a printed appointment card. One indeed, who was stone deaf, resented

receiving a typed note of her appointment signed by our secretary. One friend of our's said that he always wrote a personal note to every patient who wrote to him. This was on the advice of a very eminent Victorian surgeon, who had found that it paid to do this. Times have changed since the spacious days of the end of the last century, and nowadays nearly all appointments are made by telephone.

We always considered it a mistake to try and fit more work into the day than we felt we could honestly accomplish. Some patients very much resent being kept waiting. At times, when earlier patients have been delayed, this cannot be helped; but there is always a danger that if the surgeon be overtaxed as to time he may omit some part of the examination which could have been undertaken had there not been a number of other patients waiting to be seen.

It is a good plan to be at home for appointments only, and not to have people coming in in shoals in the expectation of being fitted in.

We remember a lady who was very angry at being kept 20 minutes for her appointment. She was so angry that she refused to accept our reasonable explanation, so at the end we suggested that she had better go away and see some one else. Her answer was—"I have already seen some one else and he kept me waiting even longer than you have done. That is why I am so angry." She was gravely ill with high blood pressure and retinal changes, so we made excuses for her and did what we could.

BOOK NOTICES

Corneal Transplantation. By B. M. FILATOF. Odessa. 1945.

Filatof published in Odessa in 1945 a book, in the first part of which, he describes and discusses his operation for transplantation of the cornea, and in the second his stimulating tissue therapy. The indications for the transplantation of the cornea are the usual ones. But the surgical technique is different. Transplantation is indicated in cases of thick leucomata, covering the whole of the cornea; the tectonic one—on partially projecting staphyloma and fistulae; cosmetic one for amelioration of the leucoma, as a preparatory step to an optical one; a reconstructive one—first proposed by Elschnig; and lastly, a therapeutic one—to heal up parts of the cornea close to the graft—really a kind of Filatof's "stimulating tissue-therapy." The surgical technique is different for some forms.

Partial total transplantation (950 cases). The purpose is to form a transparent little window through the leucoma. A special frame

is applied in the eye and face of the patient and both lids are fixed to it by sutures—so that no pressure whatever is caused in the eye. Filatof uses retrobulbar anaesthesia, subconjunctival over the superior and inferior recti. He prepares a flap of the conjunctiva 11mm. long and 8-10mm. wide After that he passes stitches through the flap and through the superior and inferior recti; he makes certain that the flap will cover the whole of the graft. After washing the donor's eye first with a solution of brilliant-green (1-500) he cuts out a disc from the centre of the eye by a special trephine and puts the trephine with the disc inside it under a glass cover. On the centre of the leucoma of the recipient a mark is made by brilliant-green with an instrument and the eye is fixed by stitches through the superior and inferior recti and by forceps, but without causing any pressure. Filatof uses a trephine, of which the important part is that its crown is first cylindrical (1mm. from the cutting edge), the canal is hermetically closed, and so the air is compressed by the disc of the cornea and the aqueous after the anterior chamber is penetrated, and so the lens is always protected by the retained aqueous. After putting a drop of 1 per cent. atropine in the wound, Filatof puts the graft on the wound by pressing down the piston of the trephine. Then the flap of the conjunctiva covers the graft, epithelium towards the cornea, and the stitches are tied first the middle one and then the two lateral ones. Then Filatof removes the stitches from the superior and inferior recti muscles, then the lid fixation sutures. Subcutaneously he injects 1 c.c. of saline into the upper and lower lid to safeguard complete closure of the lids. The binocular dressing is changed daily. In six to seven days the conjunctival sutures are removed and the conjunctival flap excised. The same operation may be performed by another type of trephine with a metallic support, and a piece of ivory with two holes; and a metallic screw to fit the ivory piece to the support. The idea is to introduce the ivory piece before trephining a hole into the anterior chamber, so that when using the trephine the lens is protected and there is a safeguard against the prolapse of the vitreous. A lance-knife with the usual angle is used, but the cutting edge is only the triangular one, the straight one is not cutting. After the knife cuts the cornea, Filatof first introduces the ivory piece, and an assistant fixes the free end of it by a hook. After the excision of the opaque cornea, the whole instrument is removed, but the ivory piece is left inside. By moving it backwards the surgeon brings its larger hole against the wound, inspects the interior of the eye, removes pieces of the iris or the capsule of the lens and again moves the ivory piece into the initial position. The extraction of an opaque lens is left till later on. The graft, prepared as in the first operation, is put into the wound, the flap of conjunctiva is replaced, etc., as described above. If the operation is performed without the ivory piece, Filatof uses his

obturators. After trephining, the surgeon introduces an obturator, raises it so that the disc closes the wound, introduces the knife behind the obturator, then introduces the ivory piece, removes the obturator and proceeds as described above.

Post-operative complications are—keratitis and iridocyclitis and glaucoma (the latter 30 per cent.). Filatof uses as donors the living and the cadaver cornea. The cadaver eye is usually kept for a few days (1 to 3) at a temperature of 2-4° above zero; he does not use the eye of a person who has suffered from syphilis, or malignant neoplasms.

The operation for amelioration or partial (by layers) transplantation is done by Graefe's knife and by special knives of Filatof. The layers of the leucoma are cut off until iris or the pupil can be seen. Then the graft is cut from a cadaver's eye in a similiar way and is put into the wound. The rest of the operation is as described above.

Cirurgia Ocular. By H. ARRUGA. Roy. 8vo., pp. XXXI, +888 with 1218 illustrations, 119 in colour. Salvat Editores S.A. Barcelona: Buenos Aires. 1946.

This is a veritable *magnum opus* of Dr. Arruga, who has returned to Spain and dates his preface from Barcelona.

The are two ways in which a text-book on operative surgery can be written: one is that in which the author describes his own procedures, giving little if any attention to alternative methods; the second is that which includes all those that custom has established as sound. The present work is of the latter kind though it is based for the most part on Arruga's own methods of practice.

The descriptions of the various operations are very full and the admirable illustrations fully portray each step. The surgery of the lens occupies 131 pages and that of retinal detachment 94. The latter chapter is superlatively good and the fine coloured illustrations, of which there are a great number, add greatly to its value.

Each section of the work includes a full bibliography, and that this is up-to-date is evidenced by the fact that several references to papers which have appeared in contemporary British and American journals of the war years are included. The book is well bound and well printed on art paper. When, as in this instance, the number of illustrations exceeeds the number of pages no other kind of paper would have been suitable. It is a credit to its distinguished author, and to his publishers, and to Spanish ophthalmology in general, including Latin America.

British and American surgeons would we feel sure welcome an English translation of it and we hope that the author will see his way to providing one.

CORRESPONDENCE

MISTER or DOCTOR

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—Although strictly speaking the title of Doctor should be confined to those who *are* "Doctors," *i.e.* those who hold the degree of Doctor of a University, yet since this title is now so universally applied to any duly qualified medical practitioner I agree with the writer of the annotation on the above subject that it is questionable whether this "Mister - Doctor" distinction subserves any useful purpose now, although it may have done in the past in the days when the Surgeon was a sort of "plumber" called in by the Physician to do a piece of technical manual work.

As I see it the chief disadvantages of the use of the term "Mister" as applied to a Surgeon are:—

1. It is confusing to the lay public.
2. It is confusing to our medical colleagues in other countries.
3. It "covers" the "unqualified" medical practitioner, for how can the layman easily distinguish (if he wishes to do so) between two gentlemen with West End addresses in the Medical area, one being a reputable Surgeon medically qualified, the other being a not-medically-qualified "naturopath," both styling themselves "Mister"?

Similarly how can the layman easily distinguish between a medically qualified ophthalmologist and an optical practitioner or ophthalmic optician, if both are just "Mister."

Now that we are on the eve of the establishment of a State Medical Service in which it is envisaged that sight testing opticians will take their official place, I would advocate that the medical men in the ophthalmic profession should for the sake of differentiation style themselves Doctor instead of Mister (just as they do in Scotland and also in Manchester).

I might add that I have no personal feelings on the subject and could not care less whether I am addressed as Mister, Doctor or just

Yours truly,

KEITH LYLE.

42, CHARLES STREET, W.1.
30th January, 1947.

MEPACRIN AND THE EYE

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—Miss Ida Mann in her communication "Blue Haloes in Atebrin Workers" has solved the clinical appearance of what

was at one time a diagnostic problem among African troops in India. The self-inflicted ocular injury caused by putting powdered mepacrin in the conjunctival sac. Although it was by that time well recognised, the first case I saw was shown to me in the summer of 1945 by Major A. E. Wilson, Ophthalmic Specialist of 135 West African General Hospital. His very accurate description of this case is as follows. "The bulbar conjunctiva was stained in an area surrounding the limbus and extending laterally in an area corresponding with the palpebral fissure. The bulbar conjunctiva above and below were devoid of any staining and the lines of demarcation above and below were sharp. The palpebrae were clear apart from narrow bands at the posterior aspects of the lid margins. The cornea was hazy and had a yellow-green colouration as if fluourescein had been inserted into the conjunctival sac and had been incompletely washed out." Major Wilson had already made the diagnosis and having searched the soldier's kit had found a yellow powder which proved to be mepacrin. He later removed a portion of the affected conjunctiva and on chemical test it gave a positive test for mepacrin. The yellow staining in the cornea disappeared after, I think, some weeks. A number of these cases were seen both by Major Wilson and by Major Hollingsworth (40 West African General Hospital) among African troops. Both these specialists reported that there was a mild conjunctivitis in the early stages and that in some a striate keratitis was present. No haloes were complained of as far as I know.

One of the diagnostic difficulties in these cases was the fact that although the mepacrin powder was presumably put in the lower fornix the conjunctival staining, with its definite edges, was limited to the interpalpebral zone of the bulbar conjunctiva. Thus it appears that exposure, possibly associated with oxygen intake. may play an essential part in the ability of the cells to take up the staining granules. The narrow yellow line on the conjunctiva of the lower lid margin was very noticeable and not easily explained either. The "striate keratitis" noticed in some cases is no doubt the same as the corneal oedema produced by massive local application in Miss Mann's experiments.

As a self-inflicted injury this procedure was successful for in a country with a high incidence of jaundice some delay was inevitable before the diagnosis could be established, thus affording the soldier the change and rest that he desired.

Yours truly,

L. B. SOMERVILLE-LARGE.

2, FITZWILLIAM PLACE,
DUBLIN.

January 28, 1947.